WEST Search History

09/925,970

DATE: Monday, October 06, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB; PLUR=YES; OP=ADJ			
L39	(L38 and L37) AnD ((@pd > 20030317)!)	33	L39
L38	((tumor necrosis factor) or tnf) AnD ((@pd > 20030317)!)	3994	L38
L37	(L36 and hepatitis) AnD ((@pd > 20030317)!)	50	L37
L36	((424/141.1)!.CCLS. or 424/133.1.ccls. or 514/2.ccls.) AnD ((@pd > 20030317)!)	246	L36
DB=USPT; PLUR=YES; OP=ADJ			
L35	(L34 and L33) AnD ((@pd > 20030317)!)	35	L35
L34	((tumor necrosis factor) or tnf) AnD ((@pd > 20030317)!)	981	L34
L33	(hepatitis and L32) AnD ((@pd > 20030317)!)	62	L33
L32	((424/141.1)!.CCLS. or 424/133.1.ccls. or 514/2.ccls.) AnD ((@pd > 20030317)!)	328	L32
DB=JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ			
L31	(infliximab or etanercept) AnD ((@pd > 20030317)!)	14	L31
DB=PGPB; PLUR=YES; OP=ADJ			
L30	(L29 and L16) AnD ((@pd > 20030317)!)	48	L30
L29	(L28 and L17) AnD ((@pd > 20030317)!)	1175	L29
L28	(L27 or L24) AnD ((@pd > 20030317)!)	1270	L28
L27	(L25 and L26) AnD ((@pd > 20030317)!)	1220	L27
L26	(L22 or L23) AnD ((@pd > 20030317)!)	3994	L26
L25	(L18 or L19 or L20 or L21) AnD ((@pd > 20030317)!)	1280	L25
L24	(etanercept or infliximab) AnD ((@pd > 20030317)!)	199	L24
L23	(tnf) AnD ((@pd > 20030317)!)	3336	L23
L22	(tumor necrosis factor) AnD ((@pd > 20030317)!)	2108	L22

L21	(tnf same inhibitor) AnD ((@pd > 20030317)!)	758	L21
L20	(tnf same antagonist) AnD ((@pd > 20030317)!)	486	L20
L19	(necrosis same antagonist) AnD ((@pd > 20030317)!)	312	L19
L18	(necrosis same inhibitor) AnD ((@pd > 20030317)!)	507	L18
L17	(receptor or monoclonal) AnD ((@pd > 20030317)!)	12925	L17
L16	(hepatitis.ti,ab,clm.) AnD ((@pd > 20030317)!)	489	L16
DB=USPT; PLUR=YES; OP=ADJ			
L15	(L14 and L13) AnD ((@pd > 20030317)!)	6	L15
L14	(hepatitis.ti,ab,clm.) AnD ((@pd > 20030317)!)	127	L14
L13	(L12 and hepatitis) AnD ((@pd > 20030317)!)	79	L13
L12	(L11 and L10) AnD ((@pd > 20030317)!)	287	L12
L11	(receptor or monoclonal) AnD ((@pd > 20030317)!)	4786	L11
L10	(L9 and L4) AnD ((@pd > 20030317)!)	333	L10
L9	(L5 or L6 or L7 or L8) AnD ((@pd > 20030317)!)	348	L9
L8	(tnf same antagonist) AnD ((@pd > 20030317)!)	105	L8
L7	(tnf same inhibitor) AnD ((@pd > 20030317)!)	222	L7
L6	(necrosis same antagonist) AnD ((@pd > 20030317)!)	79	L6
L5	(necrosis same inhibitor) AnD ((@pd > 20030317)!)	184	L5
L4	(L3 or L2) AnD ((@pd > 20030317)!)	981	L4
L3	(tnf) AnD ((@pd > 20030317)!)	724	L3
L2	(tumor necrosis factor) AnD ((@pd > 20030317)!)	694	L2
L1	(infliximab or etanercept) AnD ((@pd > 20030317)!)	23	L1

END OF SEARCH HISTORY

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     Set  Items  Description
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? s tumor (w) necrosis (w) factor

          444178  TUMOR
          118281  NECROSIS
          504093  FACTOR
      S1   44445  TUMOR (W) NECROSIS (W) FACTOR
? s s1 and hepatitis

           44445  S1
           99406  HEPATITIS
      S2     567  S1 AND HEPATITIS
? s etanercept or infliximab

             146  ETANERCEPT
             217  INFLIXIMAB
      S3     314  ETANERCEPT OR INFLIXIMAB
? s s2 and s3

             567  S2
             314  S3
      S4       0  S2 AND S3
? s s2 and antagonist?

             567  S2
          398986  ANTAGONIST?
      S5      56  S2 AND ANTAGONIST?
? t s5/6/1-56

 5/6/1
12604908   21548474   PMID: 11689884
  Inhibition of matrix metalloproteinases blocks lethal hepatitis and
apoptosis induced by tumor necrosis factor and allows safe antitumor
therapy.
Nov 2001

 5/6/2
11664729   21417321   PMID: 11526540
  Low-molecular-weight hyaluronic acid induces nuclear factor-kappaB-depend
ent resistance against tumor necrosis factor alpha-mediated liver injury in
mice.
Sep 2001

 5/6/3
11571988   21200200   PMID: 11305608
  Possible changes in expression of chemotaxin LECT2 mRNA in mouse liver
after concanavalin A-induced hepatic injury.
Apr 2001

 5/6/4
11468321   21301729   PMID: 11408521
  In vivo inhibition of Fas ligand-mediated killing by TR6, a Fas ligand
decoy receptor.
Jul 2001

 5/6/5
11282555   21189625   PMID: 11292610
  Diphenyleneiodonium sulfate, an NADPH oxidase inhibitor, prevents early
alcohol-induced liver injury in the rat.
May 2001

 5/6/6
11141022   21127349   PMID: 11222103
  Analyzing the mechanisms of interferon-induced apoptosis using CrmA and
hepatitis C virus NS5A.
Mar 1 2001

 5/6/7
10964576   20494658   PMID: 11041260
  Hepatoprotection by human epidermal growth factor (hEGF) against
experimental hepatitis induced by D-galactosamine (D-galN) or
D-GalN/lipopolysaccharide.
Oct 2000

 5/6/8
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10904269 20565040 PMID: 11112361
A broad-spectrum caspase inhibitor blocks concanavalin A-induced hepatitis in mice.
Dec 2000

5/6/9
10896745 20443582 PMID: 10990175
Update in Sjogren syndrome.
Sep 2000

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10809829 99430058 PMID: 10498828
Enhancement by galactosamine of lipopolysaccharide(LPS)-induced tumour necrosis factor production and lethality: its suppression by LPS pretreatment.
Sep 1999

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10657840 20319251 PMID: 10861114
[Effect of anti-endotoxin therapy on vaso-active substances in decompensated liver cirrhosis]
Apr 2000

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10533547 20141229 PMID: 10675538
Tumor necrosis factor-induced lethal hepatitis: pharmacological intervention with verapamil, tannic acid, picotamide and K76COOH.
Feb 11 2000

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10483381 20122340 PMID: 10655263
Galectin-1 exerts immunomodulatory and protective effects on concanavalin A-induced hepatitis in mice.
Feb 2000

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10483245 20115515 PMID: 10648469
NO-aspirin protects from T cell-mediated liver injury by inhibiting caspase-dependent processing of Th1-like cytokines.
Feb 2000

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10402032 20021815 PMID: 10553044
Activation of caspases in lethal experimental hepatitis and prevention by acute phase proteins.
Nov 15 1999

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10382072 99413951 PMID: 10484397
Differential protective effects of Bcl-xL and Bcl-2 on apoptotic liver injury in transgenic mice.
Sep 1999

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10335819 99176902 PMID: 10079016
Prevention by rolipram of concanavalin A-induced T-cell-dependent hepatitis in mice.
Feb 19 1999

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10301760 98217202 PMID: 9558119
Disparate roles for TNF-alpha and Fas ligand in concanavalin A-induced hepatitis.
Apr 15 1998

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10288539 99428427 PMID: 10498633
Frequency and nature of cytokine gene polymorphisms in type 1 autoimmune hepatitis.
Oct 1999

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10248456 99384302 PMID: 10454581
Direct association and nuclear import of the hepatitis B virus X protein with the NF-kappaB inhibitor IkappaBalpha.
Sep 1999

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10205252 99345161 PMID: 10418820
Acetaldehyde prevents nuclear factor-kappa B activation and hepatic inflammation in ethanol-fed rats.
Jul 1999

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10157545 99278290 PMID: 10347118
Prevention of lethal acute hepatic failure by antimacrophage migration inhibitory factor antibody in mice treated with bacille Calmette-Guerin and lipopolysaccharide.
Jun 1999

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10115612 99210379 PMID: 10194182
LPS challenge in D-galactosamine-sensitized mice accounts for caspase-dependent fulminant hepatitis, not for septic shock.
Apr 1999

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10012574 99113770 PMID: 9916732
Alleviation of lipopolysaccharide-induced acute liver injury in Propionibacterium acnes-primed IFN-gamma-deficient mice by a concomitant reduction of TNF-alpha, IL-12, and IL-18 production.
Jan 15 1999

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09981864 99057893 PMID: 9837909
The hepatitis B virus HBx protein inhibits caspase 3 activity.
Dec 11 1998

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09963260 98394628 PMID: 9727645
Tumor necrosis factor and alcoholic liver disease.
Aug 1998

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09916506 98439620 PMID: 9768684
Change of peripheral levels of pituitary hormones and cytokines after injection of interferon (IFN)-beta in patients with chronic hepatitis C.
Oct 1998

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09864590 98359682 PMID: 9696493
Pentoxifylline prevents concanavalin A-induced hepatitis by reducing tumor necrosis factor alpha levels and inhibiting adhesion of T lymphocytes to extracellular matrix.
Jul 1998

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09659952 98113191 PMID: 9442069
Inhibition of tumor necrosis factor (TNF-alpha)-mediated apoptosis by hepatitis C virus core protein.
Jan 23 1998

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09590973 97434732 PMID: 9288600
Interleukin-1 receptor antagonist plasma concentration is specifically increased by alpha-2A-interferon treatment.
Aug 1997

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09555980 97372490 PMID: 9228717
Increased in vitro immunosuppressive action of anti-CMV and anti-HBs intravenous immunoglobulins due to higher amounts of interferon-gamma specific neutralizing antibodies.
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09553238 97370103 PMID: 9226479
Vesnarinone inhibits immune-mediated but not Fas (CD95) agonist-mediated hepatic injury.
Jan 1997

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09456098 97131716 PMID: 8977217

Involvement of 26-kDa cell-associated TNF-alpha in experimental hepatitis and exacerbation of liver injury with a matrix metalloproteinase inhibitor.
Jan 1 1997

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09401826 97244064 PMID: 9088875
Efficacy of a selective histamine H2 receptor agonist, dimaprit, in experimental models of endotoxin shock and hepatitis in mice.
Mar 12 1997

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09352147 97329244 PMID: 9185757
Production and role of interleukin-10 in concanavalin A-induced hepatitis in mice.
Jun 1997

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09243917 97083597 PMID: 8929555
Endotoxin-inducible granulocyte-mediated hepatocytotoxicity requires adhesion and serine protease release.
Nov 1996

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09204033 97014125 PMID: 8860960
Protective effect of celosian, an acidic polysaccharide, on chemically and immunologically induced liver injuries.
Apr 1996

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09089389 96260996 PMID: 8992608
Histopathology of acetaminophen-induced liver changes: role of interleukin 1 alpha and tumor necrosis factor alpha.
Mar-Apr 1996

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08927895 96243186 PMID: 8675184
Critical involvement of interferon gamma in the pathogenesis of T-cell activation-associated hepatitis and regulatory mechanisms of interleukin-6 for the manifestations of hepatitis.
Jun 1996

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08846777 96212832 PMID: 8625746
Role of platelet-activating factor in pathogenesis of galactosamine-lipopolysaccharide-induced liver injury.
May 1996

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08763807 95111127 PMID: 7811997
Interferon-alpha induces circulating tumor necrosis factor receptor p55 in humans.
Jan 15 1995

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08560308 95341179 PMID: 7616110
Preparation of specific antibodies against murine IL-1ra and the establishment of IL-1ra as an endogenous regulator of bacteria-induced fulminant hepatitis in mice.
Jul 1995

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08495975 95237290 PMID: 7720792
Tunicamycin potently inhibits tumor necrosis factor-induced hepatocyte apoptosis.
Jan 13 1995

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08318368 95109670 PMID: 7810656
Interleukin-6 inhibits hepatocyte taurocholate uptake and sodium-potassium-adenosinetriphosphatase activity.
Dec 1994

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08250328 95008348 PMID: 7923888
Circulating proinflammatory cytokines (IL-1 beta, TNF-alpha, and IL-6) and IL-1 receptor antagonist (IL-1Ra) in fulminant hepatic failure and

acute hepatitis.
Oct 1994

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08242388 94380096 PMID: 8093093
Protection by sinomenine against endotoxin-induced fulminant hepatitis in galactosamine-sensitized mice.
Aug 30 1994

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08075562 93319538 PMID: 8392340
Protection by phosphodiesterase inhibitors against endotoxin-induced liver injury in galactosamine-sensitized mice.
Jun 22 1993

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08072996 93252184 PMID: 8387437
Effects of cytokines on HLA class I antigen expression on Huh6 and HB611 cells.
Apr 1993

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07967631 94072001 PMID: 8250973
Suppression of lipopolysaccharide-induced fulminant hepatitis and tumor necrosis factor production by bisbenzylisoquinoline alkaloids in bacillus Calmette-Guerin-treated mice.
Nov 17 1993

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07947274 94041198 PMID: 8225219
Circulating interleukin-1 and tumor necrosis factor antagonists in liver disease.
Nov 1993

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07836476 92009022 PMID: 1916153
Significance of tumor necrosis factor (TNF) and interleukin-1 (IL-1) in the pathogenesis of fulminant hepatitis: possible involvement of serine protease in TNF-mediated liver injury.
Aug 1991

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07823497 91025122 PMID: 2222515
In vivo evidence for protease-catalysed mechanism providing bioactive tumor necrosis factor alpha.
Oct 1 1990

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07718263 93114373 PMID: 1335420
Protective effects of E3330, a novel quinone derivative, on galactosamine/tumor necrosis factor-alpha-induced hepatitis in mice.
Dec 8 1992

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07674468 93113428 PMID: 1472981
Ornithine and histidine decarboxylase activities in mice sensitized to endotoxin, interleukin-1 or tumour necrosis factor by D-galactosamine.
Nov 1992

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07145507 94013465 PMID: 8408620
Cultured human liver fat-storing cells produce monocyte chemotactic protein-1. Regulation by proinflammatory cytokines.
Oct 1993

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05555467 89134308 PMID: 2465008
Tumor necrosis factor is a terminal mediator in galactosamine/endotoxin-induced hepatitis in mice.
Feb 15 1989
? t s5/9/6,12,19,26,29

5/9/6
DIALOG(R)File 155:MEDLINE(R)

11141022 21127349 PMID: 11222103
Analyzing the mechanisms of interferon-induced apoptosis using CrmA and hepatitis C virus NS5A.
Ezelle HJ; Balachandran S; Sicheri F; Polyak SJ; Barber GN
Department of Microbiology and Immunology, University of Miami School of Medicine, Miami, Florida 33136, USA.
Virology (United States) Mar 1 2001, 281 (1) p124-37, ISSN 0042-6822 Journal Code: XEA
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Subfile: INDEX MEDICUS
The dsRNA-dependent protein kinase, PKR, is a key component of interferon (IFN)-mediated anti-viral action and is frequently inhibited by many viruses following infection of the cell. Recently, we have demonstrated that IFN and PKR can sensitize cells to apoptosis predominantly through the FADD/caspase-8 pathway (S. Balachandran, P. C. Roberts, T. Kipperman, K. N. Bhalla, R. W. Compans, D. R. Archer, and G. N. Barber. (2000b) J. Virol. 74, 1513-1523). Given these findings, it is thus plausible that rather than specifically target IFN-inducible genes such as PKR, viruses could also subvert the mechanisms of IFN action, in part, at locations that could block the apoptotic cascade. To explore this possibility, we analyzed whether the poxvirus caspase-8 inhibitor, CrmA, was able to inhibit IFN or PKR/dsRNA-mediated apoptosis. Our findings indicated that CrmA could indeed inhibit apoptosis induced by both viral infection and dsRNA without blocking PKR activity or inhibiting IFN signaling. In contrast HCV-encoded NS5A, a putative inhibitor of PKR, did not appear to inhibit cell death mediated by a number of apoptotic stimuli, including IFN, TRAIL, and etoposide. Our data imply that viral-encoded inhibitors of apoptosis, such as CrmA, can block the innate arms of the immune response, including IFN-mediated apoptosis, and therefore potentially constitute an alternative family of inhibitors of IFN action in the cell. Copyright 2001 Academic Press.
Tags: Human
Descriptors: *Apoptosis--drug effects--DE; *Hepatitis C-Like Viruses; *Interferons--pharmacology--PD; *Serpins--metabolism--ME; *Viral Nonstructural Proteins--metabolism--ME; Amino Acid Substitution; Antigens, CD95--metabolism--ME; Blotting, Western; Carrier Proteins--physiology--PH; Caspases--antagonists and inhibitors--AI; Caspases--metabolism--ME; Cysteine Proteinase Inhibitors--metabolism--ME; Doxycycline--pharmacology--PD; Etoposide--pharmacology--PD; Gene Expression--drug effects--DE; Hela Cells; Interferons--antagonists and inhibitors--AI; Kinetics; Membrane Glycoproteins--pharmacology--PD; Oligonucleotide Array Sequence Analysis; Phosphorylation; RNA, Double-Stranded--pharmacology--PD; Signal Transduction--drug effects--DE; Tetracycline--pharmacology--PD; Tumor Necrosis Factor--pharmacology--PD; Vesicular Stomatitis-Indiana Virus--physiology--PH; eIF-2 Kinase--antagonists and inhibitors--AI; eIF-2 Kinase--metabolism--ME
CAS Registry No.: 0 (Antigens, CD95); 0 (Carrier Proteins); 0 (Cysteine Proteinase Inhibitors); 0 (MORT1 protein); 0 (Membrane Glycoproteins); 0 (NS-5 protein, hepatitis C virus); 0 (RNA, Double-Stranded); 0 (Serpins); 0 (TNF-related apoptosis-inducing ligand); 0 (Tumor Necrosis Factor); 0 (Viral Nonstructural Proteins); 33419-42-0 (Etoposide); 564-25-0 (Doxycycline); 60-54-8 (Tetracycline); 9008-11-1 (Interferons); 96282-35-8 (interleukin-1beta-converting enzyme inhibitor)
Enzyme No.: EC 2.7.10.- (eIF-2 Kinase); EC 3.4.22.- (Caspases); EC 3.4.22.- (caspase 8)
Record Date Created: 20010306

5/9/12
DIALOG(R)File 155:MEDLINE(R)

10533547 20141229 PMID: 10675538
Tumor necrosis factor-induced lethal hepatitis: pharmacological intervention with verapamil, tannic acid, picotamide and K76COOH.
Van Molle W; Vanden Berghe J; Brouckaert P; Libert C
Department of Molecular Biology, Flanders Interuniversity Institute for Biotechnology, University of Gent, K.L. Ledeganckstraat 35, B-9000, Gent, Belgium.
FEBS letters (NETHERLANDS) Feb 11 2000, 467 (2-3) p201-5, ISSN 0014-5793 Journal Code: EUH
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Subfile: INDEX MEDICUS

Tumor necrosis factor (TNF) induces hepatitis when injected in human beings or in rodents. The molecular mechanism by which TNF induces hepatic distress remains largely unknown, although induction of apoptosis of hepatocytes appears to be an essential step. In order to increase the therapeutic value of TNF, we have studied the protective activity of several molecules and found that four chemically totally different substances confer significant protection in the model of TNF-induced lethal hepatitis in mice sensitized with D-(+)-galactosamine (GalN), but not in mice sensitized with actinomycin-D (ActD) or against anti-Fas-induced lethal hepatitis. Verapamil, a calcium-channel blocker, tannic acid, picotamide, a thromboxane A(2) receptor antagonist, and K76COOH, an inhibitor, amongst others, of complement, protected significantly against induction of lethality, release of the liver-specific enzyme alanine aminotransferase (ALT) and induction of apoptosis in the liver after TNF/GalN, except for K76COOH, which paradoxically increased ALT values after challenge, and which also protected against TNF/GalN in complement-deficient mice. The data suggest that activation of platelets and neutrophils, as well as induction of inflammation occur in the TNF/GalN model, but not in the TNF/ActD or anti-Fas models, in which direct induction of apoptosis of hepatocytes may be more relevant. The protective activity of the drugs may lead to an increase in therapeutic value of TNF.

Tags: Animal; Support, Non-U.S. Gov't

Descriptors: *Hepatitis, Toxic--drug therapy--DT; *Phthalic Acids --pharmacology--PD; *Sesquiterpenes--pharmacology--PD; *Tannic Acid --pharmacology--PD; *Tumor Necrosis Factor--toxicity--TO; *Verapamil --pharmacology--PD; Alanine Transaminase--blood--BL; Apoptosis; Astringents --pharmacology--PD; Complement Inactivators--pharmacology--PD; Dactinomycin --administration and dosage--AD; Disease Models, Animal; Galactosamine --administration and dosage--AD; Hepatitis, Toxic--blood--BL; Hepatitis, Toxic--etiology--ET; Liver--drug effects--DE; Liver--pathology--PA; Mice; Mice, Inbred C57BL; Mice, Inbred DBA; Platelet Aggregation Inhibitors --pharmacology--PD; Tumor Necrosis Factor--administration and dosage--AD

CAS Registry No.: 0 (Astringents); 0 (Complement Inactivators); 0 (Phthalic Acids); 0 (Platelet Aggregation Inhibitors); 0 (Sesquiterpenes); 0 (Tannic Acid); 0 (Tumor Necrosis Factor); 32828-81-2 (picotamide); 50-76-0 (Dactinomycin); 52-53-9 (Verapamil); 71117-22-1 (K 76 carboxylic acid); 7535-00-4 (Galactosamine)

Enzyme No.: EC 2.6.1.2 (Alanine Transaminase)

Record Date Created: 20000331

5/9/19

DIALOG(R)File 155:MEDLINE(R)

10288539 99428427 PMID: 10498633

Frequency and nature of cytokine gene polymorphisms in type 1 autoimmune hepatitis.

Cookson S; Constantini PK; Clare M; Underhill JA; Bernal W; Czaja AJ; Donaldson PT

Institute of Liver Studies, King's College Hospital, London, UK.

Hepatology (UNITED STATES) Oct 1999, 30 (4) p851-6, ISSN 0270-9139 Journal Code: GBZ

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Subfile: INDEX MEDICUS

Genetic involvement in type 1 autoimmune hepatitis (AIH) is indicated by a marked female preponderance and strong, well-established, human leukocyte antigen (HLA) associations. These associations, however, are not universal and a number of genes outside the major histocompatibility complex may also play a role in susceptibility to type 1 AIH. Prime candidates at present are those polymorphic genes encoding the proinflammatory and immunoregulatory cytokines. The aim of this study was to investigate, for the first time, 2 members of the interleukin-1 (IL-1) family (IL-1B and IL-1RN), 3 polymorphic sites in the interleukin-10 (IL-10) gene promoter (positions -1082, -819, and -592), and 2 polymorphisms in the tumor necrosis factor-alpha (TNF-alpha) promoter (positions -308 and -238) in type 1 AIH. The study was performed on 2 independently collected DNA banks, each with appropriate controls, and throughout the analysis associations described in the first set were confirmed in the second set. Standard polymerase chain reaction (PCR)-based genotyping techniques were used. Overall there were no significant differences in the distributions of the IL-1B and IL-10 alleles, genotypes, or haplotypes in either study set. In contrast we report a significant association between type 1 AIH and TNF*2 (first set: 34% of controls vs. 49% of patients, Pc =.014 and second set: 26% vs. 56%, P =.00008). However, TNF*2 is found in strong linkage disequilibrium with the HLA A1-B8-DR3 haplotype and stratification analysis

(NF-kappa B); 0 (Tumor Necrosis Factor); 53-03-2 (Prednisone); 59122-46-2 (Misoprostol)
Record Date Created: 19981216

5/9/29
DIALOG(R)File 155:MEDLINE(R)

09659952 98113191 PMID: 9442069
Inhibition of tumor necrosis factor (TNF-alpha)-mediated apoptosis by hepatitis C virus core protein.
Ray RB; Meyer K; Steele R; Shrivastava A; Aggarwal BB; Ray R
Division of Infectious Diseases and Immunology, Saint Louis University, Missouri 63110, USA.
Journal of biological chemistry (UNITED STATES) Jan 23 1998, 273 (4) p2256-9, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: AI-45250, AI, NIAID; CA52799, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Subfile: INDEX MEDICUS
Hepatitis C virus (HCV) putative core protein has displayed many intriguing biological properties. Since tumor necrosis factor (TNF) plays an important role in controlling viral infection, in this study the effect of the core protein was investigated on the TNF-alpha induced apoptosis of human breast carcinoma cells (MCF7). HCV core protein when expressed inhibited TNF-alpha-induced apoptotic cell death unlike the control MCF7 cells, as determined by cell viability and DNA fragmentation analysis. Additionally, HCV core protein blocked the TNF-induced proteolytic cleavage of the death substrate poly(ADP-ribose) polymerase from its native 116-kDa protein to the characteristic 85-kDa polypeptide. Results from this study suggest that the HCV core protein plays a role in the inhibition of TNF-alpha-mediated cell death. Thus, the ability of core protein to inhibit the TNF-mediated apoptotic signaling pathway may provide a selective advantage for HCV replication, allowing for evasion of host antiviral defense mechanisms.
Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Descriptors: *Apoptosis--drug effects--DE; *Tumor Necrosis Factor --antagonists and inhibitors--AI; *Viral Core Proteins--pharmacology--PD; DNA Fragmentation; NAD+ ADP-Ribosyltransferase--metabolism--ME; Transfection; Tumor Cells, Cultured; Viral Core Proteins--genetics--GE
CAS Registry No.: 0 (Tumor Necrosis Factor); 0 (Viral Core Proteins); 0 (hepatitis C virus nucleocapsid protein)
Enzyme No.: EC 2.4.2.30 (NAD+ ADP-Ribosyltransferase)
Record Date Created: 19980303

? s s3 and (hepatitis or liver)

314 S3
99406 HEPATITIS
509292 LIVER
S6 7 S3 AND (HEPATITIS OR LIVER)
? t s6/6/1-7

6/6/1
12611645 21563457 PMID: 11707060
Pharmacokinetic considerations in the treatment of inflammatory bowel disease.
2001

6/6/2
12526475 21389137 PMID: 11498743
Treatment of severe steroid refractory acute graft-versus-host disease with infliximab, a chimeric human/mouse antiTNFalpha antibody.
Jul 2001

6/6/3
11816737 21563457 PMID: 11707060
Pharmacokinetic considerations in the treatment of inflammatory bowel disease.
2001

6/6/4
11661793 21399188 PMID: 11508453
Hepatitis with interface inflammation and IgG, IgM, and IgA anti-double-stranded DNA antibodies following infliximab therapy: comment on the article by Charles et al.

Aug 2001

6/6/5
11260675 21140888 PMID: 11246620
Infliximab therapy for Crohn's disease in the presence of chronic hepatitis C infection.
Feb 2001

6/6/6
10964098 20535798 PMID: 11085348
Comparative tolerability of treatments for inflammatory bowel disease.
Nov 2000

6/6/7
10921741 21028513 PMID: 11155419
Infliximab-associated reversible cholestatic liver disease.
Jan 2001
? t s6/9/1-7

6/9/1
DIALOG(R)File 155:MEDLINE(R)

12611645 21563457 PMID: 11707060
Pharmacokinetic considerations in the treatment of inflammatory bowel disease.
Schwab M; Klotz U
Dr Margarete Fischer-Bosch Institute of Clinical Pharmacology, Stuttgart, Germany.
Clinical pharmacokinetics (New Zealand) 2001, 40 (10) p723-51, ISSN 0312-5963 Journal Code: 7606849
Languages: ENGLISH
Document type: Journal Article
Record type: In Process
Subfile: INDEX MEDICUS
This review describes the pharmacokinetics of the major drugs used for the treatment of inflammatory bowel disease. This information can be helpful for the selection of a particular agent and offers guidance for effective and well tolerated regimens. The corticosteroids have a short elimination half-life (t1/2beta) of 1.5 to 4 hours, but their biological half-lives are much longer (12 to 36 hours). Most are moderate or high clearance drugs that are hepatically eliminated, primarily by cytochrome P450 (CYP) 3A4-mediated metabolism. Prednisone and budesonide undergo presystemic elimination. Any disease state or comedication affecting CYP3A4 activity should be taken into account when prescribing corticosteroids. Depending on the preparation used, 10 to 50% of an oral or rectal dose of mesalazine is absorbed. Rapid acetylation in the intestinal wall and liver (t1/2beta 0.5 to 2 hours) and transport probably by P-glycoprotein affect mucosal concentrations of mesalazine, which apparently determine clinical response. Any clinical condition influencing the release and topical availability of mesalazine might modify its therapeutic potential. Metronidazole has high (approximately 90%) oral bioavailability, with hepatic elimination characterised by a t1/2beta of 6 to 10 hours and a total clearance of about 4 L/h/kg. Ciprofloxacin is largely excreted unchanged both renally (about 45% of dose) and extrarenally (25%), with a relatively short t1/2beta (3.5 to 7 hours). Thus, renal function affects the systemic availability of ciprofloxacin. Both mercaptopurine and its prodrug azathioprine are metabolised to active compounds (6-thioguanine nucleotides; 6-TGN) by hypoxanthine-guanine phosphoribosyltransferase and to inactive metabolites by the polymorphically expressed thiopurine S-methyltransferase (TPMT) and xanthine oxidase. Patients with low TPMT activity have a higher risk of developing haemopoietic toxicity. Both mercaptopurine and azathioprine have a short t1/2beta (1 to 2 hours), but the t1/2beta of 6-TGN ranges from 3 to 13 days. Therapeutic response seems to be related to 6-TGN concentration. Almost complete bioavailability has been observed after intramuscular and subcutaneous administration of methotrexate, which is predominantly (85%) excreted as unchanged drug with a t1/2beta of up to 50 hours. Thus, renal function is the major determinant for disposition of methotrexate. Cyclosporin is slowly and incompletely absorbed. It is extensively metabolised by CYP3A4/5 in the liver and intestine (median t1/2beta and clearance 7.9 hours and 0.46 L/h/kg, respectively), and inhibitors and inducers of CYP3A4 can modify response and toxicity. Infliximab is predominantly distributed to the vascular compartment and eliminated with a t1/2beta between 10 and 14 days. No accumulation was observed when it was administered at intervals of 4 or 8 weeks. Methotrexate may reduce the clearance of infliximab from serum.
Record Date Created: 20011114

6/9/2
DIALOG(R)File 155:MEDLINE(R)

12526475 21389137 PMID: 11498743
Treatment of severe steroid refractory acute graft-versus-host disease with infliximab, a chimeric human/mouse antiTNFalpha antibody.
Kobbe G; Schneider P; Rohr U; Fenk R; Neumann F; Aivado M; Dietze L; Kronenwett R; Hunerliturkoglu A; Haas R
Department of Haematology, Oncology and Clinical Immunology, Heinrich Heine University Dusseldorf, Germany.
Bone marrow transplantation (England) Jul 2001, 28 (1) p47-9, ISSN 0268-3369 Journal Code: 8702459
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Subfile: INDEX MEDICUS
Acute graft-versus-host disease (aGVHD) is a serious complication of allogeneic peripheral blood stem cell transplantation (PBSCT). Patients with severe aGVHD not responding to treatment with steroids have a poor prognosis. We treated four patients with severe aGVHD refractory to steroids with infliximab, a chimeric human/mouse antiTNFalpha antibody. Patients (CML 2, MM 1, AML 1) developed grade III-IV GVHD at a median of 34 days (range 15-76) after myeloablative PBSCT (two), donor lymphocyte infusion for relapsed CML (one) or non-myeloablative PBSCT (one), respectively. All patients had severe intestinal involvement in addition to skin and/or liver disease and had received treatment with high-dose steroids (four) for a median of 11 days (range 5-17) in addition to CsA (four) and MMF (three). Infliximab (10 mg/kg) was given once a week until clinical improvement. In three of four patients a complete resolution of diarrhea and significant improvement of skin and liver disease were observed. Two patients received one, one patient two and one patient three infliximab infusions. At present two patients are alive >200 days after therapy, one with limited cGVHD. Two patients died, one of progressive malignant disease without GVHD and one of refractory GVHD. Infliximab is apparently an active drug for the treatment of aGVHD.
Tags: Animal; Case Report; Female; Human; Male
Descriptors: *Antibodies, Monoclonal--administration and dosage--AD; *Graft vs Host Disease--drug therapy--DT; Acute Disease; Adult; Anti-Inflammatory Agents--administration and dosage--AD; Chimeric Proteins --administration and dosage--AD; Graft vs Host Disease--pathology--PA; Hematologic Neoplasms--complications--CO; Hematologic Neoplasms--therapy --TH; Hematopoietic Stem Cell Transplantation--adverse effects--AE; Mice; Middle Age; Salvage Therapy; Steroids--therapeutic use--TU; Transplantation, Homologous--adverse effects--AE; Treatment Outcome; Tumor Necrosis Factor--immunology--IM
CAS Registry No.: 0 (Anti-Inflammatory Agents); 0 (Antibodies, Monoclonal); 0 (Chimeric Proteins); 0 (Steroids); 0 (Tumor Necrosis Factor); 0 (monoclonal antibody cA2)
Record Date Created: 20010810

6/9/3
DIALOG(R)File 155:MEDLINE(R)

11816737 21563457 PMID: 11707060
Pharmacokinetic considerations in the treatment of inflammatory bowel disease.
Schwab M; Klotz U
Dr Margarete Fischer-Bosch Institute of Clinical Pharmacology, Stuttgart, Germany.
Clinical pharmacokinetics (New Zealand) 2001, 40 (10) p723-51, ISSN 0312-5963 Journal Code: DG5
Languages: ENGLISH
Document type: Journal Article
Record type: In Process
Subfile: INDEX MEDICUS
This review describes the pharmacokinetics of the major drugs used for the treatment of inflammatory bowel disease. This information can be helpful for the selection of a particular agent and offers guidance for effective and well tolerated regimens. The corticosteroids have a short elimination half-life (t1/2beta) of 1.5 to 4 hours, but their biological half-lives are much longer (12 to 36 hours). Most are moderate or high clearance drugs that are hepatically eliminated, primarily by cytochrome P450 (CYP) 3A4-mediated metabolism. Prednisone and budesonide undergo presystemic elimination. Any disease state or comedication affecting CYP3A4 activity should be taken into account when prescribing corticosteroids. Depending on the preparation used, 10 to 50% of an oral or rectal dose of

*Anti-Infective Agents--therapeutic use--TU; *Anti-Inflammatory Agents, Non-Steroidal--therapeutic use--TU; *Gastrointestinal Agents--therapeutic use--TU; *Immunosuppressive Agents--therapeutic use--TU; *Inflammatory Bowel Diseases--drug therapy--DT; Adrenal Cortex Hormones--adverse effects --AE; Adrenal Cortex Hormones--pharmacology--PD; Anti-Infective Agents --adverse effects--AE; Anti-Infective Agents--pharmacology--PD; Anti-Inflammatory Agents, Non-Steroidal--adverse effects--AE; Anti-Inflammatory Agents, Non-Steroidal--pharmacology--PD; Gastrointestina l Agents--adverse effects--AE; Gastrointestinal Agents--pharmacology--PD; Immunosuppressive Agents--adverse effects--AE; Immunosuppressive Agents --pharmacology--PD; Mesalamine--adverse effects--AE; Mesalamine --pharmacology--PD; Mesalamine--therapeutic use--TU; Prodrugs--metabolism --ME; Sulfasalazine--adverse effects--AE; Sulfasalazine--pharmacology--PD; Sulfasalazine--therapeutic use--TU
CAS Registry No.: 0 (Adrenal Cortex Hormones); 0 (Anti-Infective Agents); 0 (Anti-Inflammatory Agents, Non-Steroidal); 0 (Gastrointestinal Agents); 0 (Immunosuppressive Agents); 0 (Prodrugs); 599-79-1 (Sulfasalazine); 89-57-6 (Mesalamine)
Record Date Created: 20010207

6/9/7
DIALOG(R)File 155:MEDLINE(R)

10921741 21028513 PMID: 11155419
Infliximab-associated reversible cholestatic liver disease.
Menghini VV; Arora AS
Department of Internal Medicine, Mayo Clinic, 200 First St SW, Rochester, MN 55905, USA.
Mayo Clinic proceedings (United States) Jan 2001, 76 (1) p84-6, ISSN 0025-6196 Journal Code: LLY
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Subfile: AIM; INDEX MEDICUS
Infliximab, a novel therapy for Crohn disease, has been shown to be both safe and effective. We describe a 44-year-old woman with Crohn disease who developed jaundice after an infusion of infliximab. Multiple investigations were undertaken, cholestatic liver disease was diagnosed, and her condition improved with supportive therapy. Although likely a rare adverse event, cholestatic liver injury should be considered in patients presenting with jaundice who have received infliximab therapy.
Tags: Case Report; Female; Human
Descriptors: *Antibodies, Monoclonal--adverse effects--AE; *Antirheumatic Agents--adverse effects--AE; *Cholestasis--chemically induced--CI; *Crohn Disease--drug therapy--DT; Adult; Cholestasis--diagnosis--DI; Cholestasis --therapy--TH; Liver--pathology--PA
CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Antirheumatic Agents); 0 (monoclonal antibody cA2)
Record Date Created: 20010111

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99406 HEPATITIS
S9 0 S8 AND HEPATITIS
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56 S8
1269078 TREATMENT
S10 9 S8 AND TREATMENT
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11549950 21357433 PMID: 11464891
N7: a novel multi-modality therapy of high risk neuroblastoma (NB) in children diagnosed over 1 year of age.
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08543790 95315955 PMID: 7795612
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06241360 87017699 PMID: 3763900
"Missing" femoral condyle: an unusual sequela to neonatal osteomyelitis and septic arthritis.
Nov 1986
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          44445  S1
         398986  ANTAGONIST?
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            440  S12
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            136  S13
              7  S6
    S14     136  S13 NOT S6
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12604908 21548474 PMID: 11689884
Inhibition of matrix metalloproteinases blocks lethal hepatitis and apoptosis induced by tumor necrosis factor and allows safe antitumor therapy.
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Tauroursodeoxycholic acid protects hepatocytes from ethanol-fed rats against tumor necrosis factor-induced cell death by replenishing mitochondrial glutathione.
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Reciprocal antagonism between estrogen receptor and NF-kappaB activity in vivo.
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12526447 21386004 PMID: 11495041
The antiestrogen toremifene protects against alcoholic liver injury in female rats.
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Reciprocal antagonism between estrogen receptor and NF-kappaB activity in vivo.
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Differential protection with inhibitors of caspase-8 and caspase-3 in murine models of tumor necrosis factor and Fas receptor-mediated hepatocellular apoptosis.
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The rexinoid LG100754 is a novel RXR:PPARgamma agonist and decreases glucose levels in vivo.
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Gliotoxin stimulates the apoptosis of human and rat hepatic stellate cells and enhances the resolution of liver fibrosis in rats.
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Catecholamines decrease nitric oxide production by cytokine-stimulated hepatocytes.
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Fumonisin-induced tumor necrosis factor-alpha expression in a porcine kidney cell line is independent of sphingoid base accumulation induced by ceramide synthase inhibition.
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Short-chain ceramide regulates hepatic methionine adenosyltransferase expression.
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In vivo inhibition of Fas ligand-mediated killing by TR6, a Fas ligand decoy receptor.
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Endothelial function in patients with hyperthyroidism before and after treatment with propranolol and thiamazol.
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11375718 21190722 PMID: 11297059
Important role for endothelins in acute hepatic ischemia/reperfusion injury.
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In vivo delivery of antisense oligonucleotides in pH-sensitive liposomes inhibits lipopolysaccharide-induced production of tumor necrosis factor-alpha in rats.
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Hepatocyte toll-like receptor 2 expression in vivo and in vitro: role of cytokines in induction of rat TLR2 gene expression by lipopolysaccharide.
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Normal pharmacologically-induced, but decreased regenerative liver growth in interleukin-6-deficient (IL-6(-/-)) mice.
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Gadolinium chloride-induced hepatocyte proliferation is prevented by antibodies to tumor necrosis factor alpha.
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Bacterial lipopolysaccharide enhances aflatoxin B1 hepatotoxicity in rats by a mechanism that depends on tumor necrosis factor alpha.
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Inhibition of TNF-alpha produced by Kupffer cells protects against the nonspecific liver toxicity of immunotoxin anti-Tac(Fv)-PE38, LMB-2.
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A broad-spectrum caspase inhibitor blocks concanavalin A-induced hepatitis in mice.
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Peroxisome proliferator-activated receptors and hepatic stellate cell activation.
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Protection against TNF-induced liver parenchymal cell apoptosis during endotoxemia by a novel caspase inhibitor in mice.
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Nuclear factor kappaB in proliferation, activation, and apoptosis in rat hepatic stellate cells.
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Disulfiram inhibits TNF-alpha-induced cell death.
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Inhibition of lipopolysaccharide-induced I-kappaB degradation and tumor necrosis factor-alpha expression by acriflavine, an antimicrobial agent.
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Secretory leukocyte protease inhibitor in mice regulates local and remote organ inflammatory injury induced by hepatic ischemia/reperfusion.
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Enhancement by galactosamine of lipopolysaccharide(LPS)-induced tumour necrosis factor production and lethality: its suppression by LPS pretreatment.
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Activation of nuclear factor-kappaB during orthotopic liver transplantation in rats is protective and does not require Kupffer cells.
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Tumor necrosis factor-alpha induces hepatic insulin resistance in obese Zucker (fa/fa) rats via interaction of leukocyte antigen-related tyrosine phosphatase with focal adhesion kinase.
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Requirement for glycogen synthase kinase-3beta in cell survival and NF-kappaB activation.
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Lethal granuloma disintegration in mycobacteria-infected TNFRp55-/- mice is dependent on T cells and IL-12.

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Effects of hyperthermia and tumour necrosis factor on inflammatory cytokine secretion and procoagulant activity in endothelial cells.
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[Effect of anti-endotoxin therapy on vaso-active substances in decompensated liver cirrhosis]
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Tumor necrosis factor alpha-mediated toxic shock in Trypanosoma cruzi-infected interleukin 10-deficient mice.
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Brief hypoxia differentially regulates LPS-induced IL-1beta and TNF-alpha gene transcription in RAW 264.7 cells.
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Inhibition of hyaluronan synthesis by vesnarinone in cultured human myofibroblasts.
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Neutralization of IL-18 reduces neutrophil tissue accumulation and protects mice against lethal Escherichia coli and Salmonella typhimurium endotoxemia.
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Suppression of lethal toxicity of endotoxin by biscoclaurine alkaloid cepharanthin.
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Galectin-1 exerts immunomodulatory and protective effects on concanavalin A-induced hepatitis in mice.
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Effect of the 21-aminosteroid on nuclear factor-kappa B activation of Kupffer cells in endotoxin shock.
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Hepatocytes sensitized to tumor necrosis factor-alpha cytotoxicity undergo apoptosis through caspase-dependent and caspase-independent pathways.
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Nitric oxide and the Th2 response combine to prevent severe hepatic damage during Schistosoma mansoni infection.
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Glycyrrhizin inhibits TNF-induced, but not Fas-mediated, apoptosis in the human hepatoblastoma line HepG2.
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A metalloproteinase inhibitor prevents acute graft-versus-host disease in mice after bone marrow transplantation.
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Prevention by rolipram of concanavalin A-induced T-cell-dependent hepatitis in mice.
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S-adenosylmethionine attenuates the lipopolysaccharide-induced expression of the gene for tumour necrosis factor alpha.
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Metalloproteinase inhibitor prevents hepatic injury in endotoxemic mice.
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Inhibition of NF-kappaB activation by pyrrolidine dithiocarbamate prevents In vivo expression of proinflammatory genes.
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Endotoxin stimulates hepatocyte interleukin-6 production.
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Cytotoxicity induced by the combination of valproic acid and tumor necrosis factor-alpha: implication for valproic acid-associated hepatotoxicity syndrome.
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Acetaldehyde prevents nuclear factor-kappa B activation and hepatic inflammation in ethanol-fed rats.
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The effect of lexipafant on bacterial translocation in acute necrotizing pancreatitis in rats.
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Ceramide induces caspase-independent apoptosis in rat hepatocytes sensitized by inhibition of RNA synthesis.
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Prevention of lethal acute hepatic failure by antimacrophage migration inhibitory factor antibody in mice treated with bacille Calmette-Guerin and lipopolysaccharide.
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LPS challenge in D-galactosamine-sensitized mice accounts for caspase-dependent fulminant hepatitis, not for septic shock.
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Glycine and uridine prevent D-galactosamine hepatotoxicity in the rat: role of Kupffer cells.
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Endogenous glucocorticoids released during acute toxic liver injury enhance hepatic IL-10 synthesis and release.
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Different efficacy of soluble CD14 treatment in high- and low-dose LPS models.
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Zonated expression of cytokines in rat liver: effect of chronic ethanol and the cytochrome P450 2E1 inhibitor, chlormethiazole.
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Protective effects of a human 18-kilodalton cationic antimicrobial protein (CAP18)-derived peptide against murine endotoxemia.
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A dichotomous role for nitric oxide during acute Toxoplasma gondii infection in mice.
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Interleukin-1 receptor antagonist plasma concentration is specifically increased by alpha-2A-interferon treatment.
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Leukotriene D4 activates a chloride conductance in hepatocytes from lipopolysaccharide-treated rats.
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The HMC-1 human mast cell line expresses the hepatocyte growth factor receptor c-met.
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Tumor necrosis factor alpha inhibits collagen alpha 1(I) gene expression in rat hepatic stellate cells through a G protein.
Aug 1997

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Mechanism for biphasic rel A. NF-kappaB1 nuclear translocation in tumor necrosis factor alpha-stimulated hepatocytes.
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Involvement of 26-kDa cell-associated TNF-alpha in experimental hepatitis and exacerbation of liver injury with a matrix metalloproteinase inhibitor.
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Inflammatory cytokines and type I 5'-deiodinase expression in phi1 rat liver cells.
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Targeting nitric oxide (NO) delivery in vivo. Design of a liver-selective NO donor prodrug that blocks tumor necrosis factor-alpha-induced apoptosis and toxicity in the liver.
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Superantigen and endotoxin synergize in the induction of lethal shock.
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Administration of a matrix metalloproteinase inhibitor after hemorrhage improves cardiovascular and hepatocellular function.
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Apigenin inhibits tumor necrosis factor-induced intercellular adhesion molecule-1 upregulation in vivo.
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Thrombin is a distal mediator of lipopolysaccharide-induced liver injury in the rat.
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09156501 97123303 PMID: 8968550
Role of nitric oxide in the circulatory failure and organ injury in a rodent model of gram-positive shock.
Dec 1996

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09089779 97125529 PMID: 8970606
Protection by Carolina rinse solution, acidotic pH, and glycine against lethal reperfusion injury to sinusoidal endothelial cells of rat livers stored for transplantation.
Dec 15 1996

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09089389 96260996 PMID: 8992608
Histopathology of acetaminophen-induced liver changes: role of interleukin 1 alpha and tumor necrosis factor alpha.
Mar-Apr 1996

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08927896 96243187 PMID: 8675185
Thalidomide inhibits tumor necrosis factor alpha, decreases nitric oxide synthesis, and ameliorates the hyperdynamic circulatory syndrome in portal-hypertensive rats.
Jun 1996

14/6/98
08927895 96243186 PMID: 8675184
Critical involvement of interferon gamma in the pathogenesis of T-cell activation-associated hepatitis and regulatory mechanisms of interleukin-6 for the manifestations of hepatitis.
Jun 1996

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08911898 96205331 PMID: 8630016
Anti-TNF treatment reverts increased muscle ubiquitin gene expression in tumour-bearing rats.
Apr 25 1996

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08911845 96189116 PMID: 8628301
IkappaBalpha deficiency results in a sustained NF-kappaB response and severe widespread dermatitis in mice.
May 1996

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08904260 96080983 PMID: 7475981
Tumor necrosis factor-alpha and nitric oxide production in endotoxin-primed rats administered carbon tetrachloride.
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08844884 96212940 PMID: 8622628
Role of nitric oxide in the cytokine-mediated regulation of cytochrome P-450.
May 1996

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08826007 96152599 PMID: 8564931
Muscle hypercatabolism during cancer cachexia is not reversed by the glucocorticoid receptor antagonist RU38486.
Jan 19 1996

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08808639 96091812 PMID: 8586485
Reduction in endotoxin-induced organ dysfunction and cytokine secretion by a cyclic nitrone antioxidant.
Jul 1995

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08799800 96069133 PMID: 7577459
Perturbations of triglycerides but not of cholesterol metabolism are prevented by anti-tumour necrosis factor treatment in rats bearing an ascites hepatoma (Yoshida AH-130).
Nov 1995

14/6/106
08763807 95111127 PMID: 7811997
Interferon-alpha induces circulating tumor necrosis factor receptor p55 in humans.
Jan 15 1995

14/6/107
08725097 96193212 PMID: 8608396
Sepsis stimulates polyamine biosynthesis in the liver and increases tissue levels of ornithine decarboxylase mRNA.
Dec 1995

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08645424 96062041 PMID: 7589088
Lipopolysaccharide-induced interleukin-10 in mice: role of endogenous tumor necrosis factor-alpha.
Oct 1995

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08586852 95265055 PMID: 7538197
Suppression of the constitutive expression of cytochrome P-450 2C11 by cytokines and interferons in primary cultures of rat hepatocytes: comparison with induction of acute-phase genes and demonstration that CYP2C11 promoter sequences are involved in the suppressive response to interleukins 1 and 6.
May 1995

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08554917 95332746 PMID: 7608565
Inhibition of TNF-triggering activity of lipopolysaccharide by a proteinaceous factor from normal mouse liver extract.
Jul 15 1995

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08495975 95237290 PMID: 7720792
Tunicamycin potently inhibits tumor necrosis factor-induced hepatocyte apoptosis.
Jan 13 1995

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08483533 95209886 PMID: 7695925
Induction of lipopolysaccharide-binding protein gene expression in cultured rat pulmonary artery smooth muscle cells by interleukin 1 beta.
Apr 1995

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08475115 95184830 PMID: 7879175
Donor treatment with gadolinium chloride improves survival after transplantation of cold-stored livers by reducing Kupffer cell tumor necrosis factor production in rats.
Feb 1995

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08410153 94273736 PMID: 7516291
Evidence that FK506 alleviates ischemia/reperfusion injury to the rat liver: in vivo demonstration for suppression of TNF-a production in response to endotoxemia.
1994

14/6/115
08318368 95109670 PMID: 7810656
Interleukin-6 inhibits hepatocyte taurocholate uptake and sodium-potassium-adenosinetriphosphatase activity.
Dec 1994

14/6/116
08299596 95080137 PMID: 7988454
Alpha-adrenergic receptors mediate the hypertriglyceridemia induced by endotoxin, but not tumor necrosis factor, in rats.
Dec 1994

14/6/117
08269413 95035881 PMID: 7948767
Platelet-activating factor antagonists suppress the generation of tumor necrosis factor-alpha and superoxide induced by lipopolysaccharide or phorbol ester in rat liver macrophages.
May-Jun 1994

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08250328 95008348 PMID: 7923888
Circulating proinflammatory cytokines (IL-1 beta, TNF-alpha, and IL-6) and IL-1 receptor antagonist (IL-1Ra) in fulminant hepatic failure and acute hepatitis.
Oct 1994

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08207019 94325582 PMID: 8049450
Recombinant human interleukin-1 receptor antagonist in the treatment of steroid-resistant graft-versus-host disease.
Aug 15 1994

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08125577 94181598 PMID: 8134404
The effects of anti-TNF-alpha antibody and dexamethasone on TCDD-induced oxidative stress in mice.
Feb 1994

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08059729 97270011 PMID: 9114909
Effects of interferon-alpha monotherapy on hepatic drug metabolism in cancer patients.
Sep 1993

14/6/122
08005536 93234523 PMID: 7682706
Molecular cloning and expression of inducible nitric oxide synthase from human hepatocytes.
Apr 15 1993

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07989709 94109378 PMID: 8281931
Participation in cellular prostaglandin synthesis of type-II phospholipase A2 secreted and anchored on cell-surface heparan sulfate proteoglycan.
Dec 15 1993

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07626258 92349210 PMID: 1640347
Effect of interleukin-1 beta on gene expressions and functions of fibroblastic cells derived from human periodontal ligament.
Jul 1992

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07554817 92109774 PMID: 1722406
Dexamethasone prevents the growth inhibitory effects of recombinant tumor necrosis factor in a rat hepatoma cell line Reuber-RC-3: an association with the changes in the messenger RNA levels for multidrug resistance gene.
Dec 31 1991

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07212019 90201639 PMID: 2318380
Ex vivo lipopolysaccharide-induced interleukin-1 secretion from murine peritoneal macrophages inhibited by probucol, a hypocholesterolemic agent with antioxidant properties.
Apr 1 1990

14/6/127
07141330 93342631 PMID: 8342131
Interleukin-1 receptor antagonist improves survival and preserves organ adenosine-5'-triphosphate after hemorrhagic shock.
Aug 1993

14/6/128
07134431 93187535 PMID: 8445328
Endogenous nitric oxide inhibits the synthesis of cyclooxygenase products and interleukin-6 by rat Kupffer cells.
Feb 1993

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07115125 94169401 PMID: 8123873
The role of cytokines in the pathophysiology of chronic liver diseases.
1993

14/6/130
07099713 94029217 PMID: 8215636
Neutrophil and nonneutrophil-mediated injury in intestinal ischemia-reperfusion.
Oct 1993

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06905330 93081049 PMID: 1449830
The role of leukotriene D4 in septic shock models.
1992

14/6/132
06898105 93069219 PMID: 1440607
Inhibition of acute TCDD toxicity by treatment with anti-tumor necrosis factor antibody or dexamethasone.
Nov 1992

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06846910 91298579 PMID: 1712553
Interleukin-1 and tumor necrosis factor-alpha inhibit erythropoietin production in vitro.
1991

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05636966 87323476 PMID: 3115109
Toxicity of tumor necrosis factor is synergistic with gamma-interferon and can be reduced with cyclooxygenase inhibitors.
Sep 1987

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05395369 89285384 PMID: 2660586
Reversal of the toxic effects of cachectin by concurrent insulin administration.
Jun 1989

14/6/136
05295235 89341610 PMID: 2788206
Dexamethasone modulation of in vivo effects of endotoxin, tumor necrosis factor, and interleukin-1 on liver cytochrome P-450, plasma fibrinogen, and serum iron.

Sep 1989
? t s14/9/67,81,118,129
 14/9/67
DIALOG(R)File 155:MEDLINE(R)

09916506 98439620 PMID: 9768684
  Change of peripheral levels of pituitary hormones and cytokines after injection of interferon (IFN)-beta in patients with chronic hepatitis C.
  Ohno Y; Fujimoto M; Nishimura A; Aoki N
  Second Department of Medicine, Kinki University School of Medicine, Osaka-Sayama, Osaka, Japan.
  Journal of clinical endocrinology and metabolism (UNITED STATES) Oct 1998, 83 (10) p3681-7, ISSN 0021-972X Journal Code: HRB
  Languages: ENGLISH
  Document type: Clinical Trial; Controlled Clinical Trial; Journal Article
  Record type: Completed
  Subfile: AIM; INDEX MEDICUS
  Interferons (IFNs) are now in use worldwide for the treatment of chronic viral hepatitis. Unfortunately, various side effects of IFNs have been reported. Because cytokines, which include IFNs, can affect endocrine function, endocrinological abnormalities are sometimes observed in patients treated with IFNs. We examined the effects of IFN-beta on peripheral levels of pituitary and adrenal hormones and cytokines. Six million international units of IFN-beta dissolved in glucose solution was injected for 30 min. As a control study, glucose solution without IFN-beta was injected. Pituitary hormones (ACTH, GH, TSH, prolactin (PRL), LH, FSH, and arginine-vasopressin (AVP)), cortisol, and cytokines such as interleukin (IL)-1, IL-6, tumor necrosis factor-alpha (TNF), and interleukin-1 receptor antagonist (IL-1ra) were measured before and after IFN-beta injection. The study was carried out on 14 patients with chronic hepatitis type C who were under treatment with IFN-beta. All studies were performed when the patients were afebrile. None of the patients had any endocrine or autoimmune diseases. Plasma ACTH levels increased significantly at 60-120 min after IFN-beta injection compared with the levels before IFN-beta injection and in the control study using glucose injection. Plasma cortisol levels increased after IFN-beta injection, in parallel with plasma ACTH elevation. Serum GH levels increased significantly at 120 min after IFN-beta injection. All the increased hormones including ACTH, cortisol, and GH, were decreased at the end of the study-180 min after IFN-beta injection. Serum levels of TSH, PRL, LH, FSH, and AVP were not changed significantly by IFN-beta injection. Plasma IL-1 and TNF levels did not change after IFN-beta injection, while IL-6 and IL-1ra were elevated significantly. The increases in IL-6 and IL-1ra were gradual, reaching their peak levels at 180 min after IFN-beta injection. However there were no correlations between the hormones measured in this study and the levels of IL-6 or IL-1ra. It would seem that IFN-beta has direct or indirect stimulatory effects for ACTH and GH without mediation of the cytokines. These in vivo results are important for investigating the relationship between endocrine and cytokine systems in humans.
  Tags: Female; Human; Male
  Descriptors: *Antiviral Agents--therapeutic use--TU; *Cytokines--blood --BL; *Hepatitis C, Chronic--blood--BL; *Hepatitis C, Chronic--therapy--TH ; *Interferon-beta--therapeutic use--TU; *Pituitary Hormones--blood--BL; Adrenal Cortex Hormones--blood--BL; Adult; Injections; Middle Age; Treatment Outcome
  CAS Registry No.: 0 (Adrenal Cortex Hormones); 0 (Antiviral Agents); 0 (Cytokines); 0 (Pituitary Hormones); 77238-31-4 (Interferon-beta)
  Record Date Created: 19981105

 14/9/81
DIALOG(R)File 155:MEDLINE(R)

09456098 97131716 PMID: 8977217
  Involvement of 26-kDa cell-associated TNF-alpha in experimental hepatitis and exacerbation of liver injury with a matrix metalloproteinase inhibitor.
  Solorzano CC; Ksontini R; Pruitt JH; Hess PJ; Edwards PD; Kaibara A; Abouhamze A; Auffenberg T; Galardy RE; Vauthey JN; Copeland EM; Edwards CK; Lauwers GY; Clare-Salzler M; MacKay SL; Moldawer LL; Lazarus DD
  Department of Surgery, University of Florida College of Medicine, Gainesville 32610, USA.
  Journal of immunology (UNITED STATES) Jan 1 1997, 158 (1) p414-9, ISSN 0022-1767 Journal Code: IFB
  Contract/Grant No.: GM-40586, GM, NIGMS; GM-52532, GM, NIGMS
  Languages: ENGLISH
  Document type: Journal Article
  Record type: Completed

--IM; *Liver Failure, Acute--immunology--IM; *Receptors, Interleukin-1 --antagonists and inhibitors--AI; *Sialoglycoproteins--blood--BL; Adolescence; Adult; Aged; Hepatocyte Growth Factor--blood--BL; Interleukin-1--blood--BL; Interleukin-6--blood--BL; Liver Function Tests; Middle Age; Tumor Necrosis Factor--metabolism--ME
CAS Registry No.: 0 (Cytokines); 0 (Interleukin-1); 0 (Interleukin-6); 0 (Receptors, Interleukin-1); 0 (Sialoglycoproteins); 0 (Tumor Necrosis Factor); 0 (interleukin 1 receptor antagonist protein); 67256-21-7 (Hepatocyte Growth Factor)
Record Date Created: 19941108

14/9/129
DIALOG(R)File 155:MEDLINE(R)

07115125 94169401 PMID: 8123873
The role of cytokines in the pathophysiology of chronic liver diseases.
Tilg H
Department of Medicine, University Hospital Innsbruck, Austria.
International journal of clinical & laboratory research (GERMANY) 1993, 23 (4) p179-85, ISSN 0940-5437 Journal Code: A81
Languages: ENGLISH
Document type: Journal Article; Review; Review, Tutorial
Record type: Completed
Subfile: INDEX MEDICUS
Many of the biological activities of cytokines are similar to clinical manifestations and abnormalities of laboratory parameters observed in chronic liver diseases (CLD). Evidence of impaired cytokine synthesis in CLD comes from studies of serum or plasma levels, supernatants of peripheral blood mononuclear cells stimulated with various agents and from studying cytokine expression locally in the liver. Circulating levels of several cytokine-regulated molecules such as neopterin, soluble IL-2 receptor, adhesion molecules, and metabolites of the nitric oxide pathway are elevated in patients with CLD. Thus inhibition of cytokine synthesis or modulation of their activity could provide not only important information about their pathophysiologic relevance but also have a profound impact on disease progression in CLD. These studies will also show whether prolonged anti-cytokine treatment with interleukin-1- or tumor necrosis factor-inhibitors interferes with host defense mechanism. (67 Refs.)
Tags: Human
Descriptors: *Interleukin-1--physiology--PH; *Interleukin-6--physiology --PH; *Liver Diseases--physiopathology--PP; *Tumor Necrosis Factor --physiology--PH; Chronic Disease; Interleukin-1 --antagonists and inhibitors--AI; Interleukin-1--biosynthesis--BI; Interleukin-6--antagonists and inhibitors--AI; Interleukin-6--biosynthesis--BI; Liver Diseases --drug therapy--DT; Liver Diseases--metabolism--ME; Tumor Necrosis Factor --antagonists and inhibitors--AI; Tumor Necrosis Factor--biosynthesis--BI
CAS Registry No.: 0 (Interleukin-1); 0 (Interleukin-6); 0 (Tumor Necrosis Factor)
Record Date Created: 19940412

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? s s2 and treatment

             567  S2
         1269078  TREATMENT
     S15     148  S2 AND TREATMENT
? s receptor? or monoclonal

          536061  RECEPTOR?
          156808  MONOCLONAL
     S16  660762  RECEPTOR? OR MONOCLONAL
? s s15 and s16

             148  S15
          660762  S16
     S17      37  S15 AND S16
? t s17/6/1-37

 17/6/1
12610421   21555456   PMID: 11699044
  Decrease of elevated N,N-dimethylglycine and N-methylglycine in human immunodeficiency virus infection during short-term highly active antiretroviral therapy.
Nov 2001

 17/6/2
12598840   21540628   PMID: 11685033
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Protection against Fas-mediated and tumor necrosis factor receptor 1-mediated liver injury by blockade of FADD without loss of nuclear factor-kappaB activation.
Nov 2001

17/6/3
11824661 21540628 PMID: 11685033
Protection against Fas-mediated and tumor necrosis factor receptor 1-mediated liver injury by blockade of FADD without loss of nuclear factor-kappaB activation.
Nov 2001

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11808737 21555456 PMID: 11699044
Decrease of elevated N,N-dimethylglycine and N-methylglycine in human immunodeficiency virus infection during short-term highly active antiretroviral therapy.
Nov 2001

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11511707 21306055 PMID: 11413121
Tumour necrosis factor alpha impairs function of liver derived T lymphocytes and natural killer cells in patients with primary sclerosing cholangitis.
Jul 2001

17/6/6
11469715 21327737 PMID: 11433695
[Acute alcoholic hepatitis: treatments]
Hepatite alcoolique aigue: ses traitements.
Jun 9 2001

17/6/7
11468321 21301729 PMID: 11408521
In vivo inhibition of Fas ligand-mediated killing by TR6, a Fas ligand decoy receptor.
Jul 2001

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11223011 21165433 PMID: 11264022
Distinct roles of tumor necrosis factor-alpha and nitric oxide in acute liver injury induced by carbon tetrachloride in mice.
Apr 1 2001

17/6/9
10813672 20455622 PMID: 10998439
Minimal effect of cytokine-independent hepatitis induced by anti-Fas antibodies on hepatic cytochrome P450 gene expression in mice.
Oct 2000

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10785534 20459022 PMID: 11003616
Murine concanavalin A-induced hepatitis is prevented by interleukin 12 (IL-12) antibody and exacerbated by exogenous IL-12 through an interferon-gamma-dependent mechanism.
Oct 2000

17/6/11
10740454 97385174 PMID: 9238048
Hepatitis B virus HBx protein sensitizes cells to apoptotic killing by tumor necrosis factor alpha.
Aug 5 1997

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10602254 20208742 PMID: 10746953
Acute hepatotoxicant exposure induces TNFR-mediated hepatic injury and cytokine/apoptotic gene expression.
Mar 2000

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10498623 20142938 PMID: 10680745
Concanavalin A-induced hepatitis in mice is prevented by interleukin (IL)-10 and exacerbated by endogenous IL-10 deficiency.
Oct 1999

17/6/14

10483381 20122340 PMID: 10655263
Galectin-1 exerts immunomodulatory and protective effects on concanavalin A-induced hepatitis in mice.
Feb 2000

17/6/15
10335819 99176902 PMID: 10079016
Prevention by rolipram of concanavalin A-induced T-cell-dependent hepatitis in mice.
Feb 19 1999

17/6/16
10283826 99430981 PMID: 10503656
Current issues in the diagnosis and treatment of Sjogren's syndrome.
Sep 1999

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10019945 99099065 PMID: 9882379
Hepatitis C virus core protein enhances NF-kappaB signal pathway triggering by lymphotoxin-beta receptor ligand and tumor necrosis factor alpha.
Feb 1999

17/6/18
09916506 98439620 PMID: 9768684
Change of peripheral levels of pituitary hormones and cytokines after injection of interferon (IFN)-beta in patients with chronic hepatitis C.
Oct 1998

17/6/19
09864590 98359682 PMID: 9696493
Pentoxifylline prevents concanavalin A-induced hepatitis by reducing tumor necrosis factor alpha levels and inhibiting adhesion of T lymphocytes to extracellular matrix.
Jul 1998

17/6/20
09665836 98122483 PMID: 9462651
Strain difference in the induction of T-cell activation-associated, interferon gamma-dependent hepatic injury in mice.
Feb 1998

17/6/21
09590973 97434732 PMID: 9288600
Interleukin-1 receptor antagonist plasma concentration is specifically increased by alpha-2A-interferon treatment.
Aug 1997

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09588981 97466782 PMID: 9328122
Serum levels of IL-10, IL-15 and soluble tumour necrosis factor-alpha (TNF-alpha) receptors in type C chronic liver disease.
Sep 1997

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09495845 95239974 PMID: 7723241
Production of interleukin-6, tumor necrosis factor alpha and interleukin-10 in vitro correlates with the clinical immune defect in chronic hemodialysis patients.
Feb 1995

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09456098 97131716 PMID: 8977217
Involvement of 26-kDa cell-associated TNF-alpha in experimental hepatitis and exacerbation of liver injury with a matrix metalloproteinase inhibitor.
Jan 1 1997

17/6/25
09397928 97270494 PMID: 9125577
Tumor necrosis factor receptor p55 is essential for intrahepatic granuloma formation and hepatocellular apoptosis in a murine model of bacterium-induced fulminant hepatitis.
May 1997

17/6/26
09380210 97376882 PMID: 9233653

17/9/25
DIALOG(R)File 155:MEDLINE(R)

09397928 97270494 PMID: 9125577
Tumor necrosis factor receptor p55 is essential for intrahepatic granuloma formation and hepatocellular apoptosis in a murine model of bacterium-induced fulminant hepatitis.
Tsuji H; Harada A; Mukaida N; Nakanuma Y; Bluethmann H; Kaneko S; Yamakawa K; Nakamura SI; Kobayashi KI; Matsushima K
Department of Pharmacology, Cancer Research Institute, Kanazawa University, Takara-machi, Japan.
Infection and immunity (UNITED STATES) May 1997, 65 (5) p1892-8, ISSN 0019-9567 Journal Code: GO7
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Subfile: INDEX MEDICUS
Accumulating evidence implicates tumor necrosis factor (TNF) and Fas systems in liver injury, although the interaction between these two systems remains to be investigated. In this study, we examined Propionibacterium acnes-primed TNF receptor p55-deficient (TNFRp55-/-) or Fas-deficient MRL/MpJ Lpr/Lpr mice challenged with lipopolysaccharide (LPS). Priming with P. acnes caused mononuclear cell infiltration into the hepatic lobules and granuloma formation in the livers of TNFRp55 wild-type mice. Subsequent LPS challenge caused massive liver injury and a marked increase in transaminase levels, leading to acute lethality in control wild-type mice. In contrast, the same treatment caused few pathological changes in livers of TNFRp55-/- mice, and all animals survived. P. acnes and subsequent LPS challenge induced granuloma formation and apoptotic changes, respectively, in livers of MRL/MpJ Lpr/Lpr mice. However, liver injury was 50% of that in control MRL/MpJ +/+ mice, suggesting some role of the Fas-Fas ligand system in this liver injury model. On the other hand, an agonistic anti-Fas antibody caused massive apoptosis and hemorrhagic changes of the liver without any priming with P. acnes, leading to death in both TNFRp55-/- and control wild-type mice. These results suggest that TNFRp55 but not Fas was involved in P. acnes-induced granuloma formation as well as subsequent LPS-induced liver injury and that TNFRp55 and Fas independently induced apoptosis of hepatocytes in vivo.
Tags: Animal; Support, Non-U.S. Gov't
Descriptors: *Apoptosis--immunology--IM; *Gram-Positive Bacterial Infections--immunology--IM; *Gram-Positive Bacterial Infections --microbiology--MI; *Granuloma--immunology--IM; *Granuloma--microbiology --MI; *Hepatitis, Animal--immunology--IM; *Hepatitis, Animal--microbiology --MI; *Liver--immunology--IM; *Liver--microbiology--MI; *Propionibacterium acnes; *Receptors, Tumor Necrosis Factor--immunology--IM; Antibodies, Blocking--immunology--IM; Antigens, CD95--genetics--GE; Antigens, CD95 --immunology--IM; DNA Fragmentation; Enzyme-Linked Immunosorbent Assay; Kinetics; Lipopolysaccharides--immunology--IM; Liver--pathology--PA; Mice; Mice, Inbred C57BL; Mice, Inbred MRL lpr; Mice, Inbred Strains; Receptors, Tumor Necrosis Factor--genetics--GE; Time Factors; Transaminases--analysis --AN; Transaminases--blood--BL; Transaminases--metabolism--ME
CAS Registry No.: 0 (Antibodies, Blocking); 0 (Antigens, CD95); 0 (Lipopolysaccharides); 0 (Receptors, Tumor Necrosis Factor)
Enzyme No.: EC 2.6.1. (Transaminases)
Record Date Created: 19970515

17/9/27
DIALOG(R)File 155:MEDLINE(R)

09344423 97347897 PMID: 9203964
The roles of tumour necrosis factor-alpha, interleukin-1 and interleukin-12 in murine cytomegalovirus infection.
Yerkovich ST; Olver SD; Lenzo JC; Peacock CD; Price P
Department of Microbiology, University of Western Australia, Nedlands, Australia.
Immunology (ENGLAND) May 1997, 91 (1) p45-52, ISSN 0019-2805 Journal Code: GH7
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Subfile: INDEX MEDICUS
The roles of the inflammatory cytokines tumour necrosis factor-alpha (TNF-alpha), interleukin-1 (IL-1) and IL-12, in murine cytomegalovirus (MCMV) disease were investigated in susceptible BALB/c and resistant C57BL/6 mice. MCMV infection induced IL-1 and TNF-alpha production by peritoneal cells from BALB/c mice, as demonstrated previously in C57BL/6

Requirement of IL-4 and liver NK1+ T cells for concanavalin A-induced hepatic injury in mice.
Aug 1 1997

17/6/27
09344423 97347897 PMID: 9203964
The roles of tumour necrosis factor-alpha, interleukin-1 and interleukin-12 in murine cytomegalovirus infection.
May 1997

17/6/28
09242976 99265035 PMID: 10332631
Tumor necrosis factor production by rat Kupffer cells-regulation by lipopolysaccharide, macrophage activating factor and prostaglandin E2.
1996

17/6/29
09089389 96260996 PMID: 8992608
Histopathology of acetaminophen-induced liver changes: role of interleukin 1 alpha and tumor necrosis factor alpha.
Mar-Apr 1996

17/6/30
08927895 96243186 PMID: 8675184
Critical involvement of interferon gamma in the pathogenesis of T-cell activation-associated hepatitis and regulatory mechanisms of interleukin-6 for the manifestations of hepatitis.
Jun 1996

17/6/31
08763807 95111127 PMID: 7811997
Interferon-alpha induces circulating tumor necrosis factor receptor p55 in humans.
Jan 15 1995

17/6/32
08501372 95246979 PMID: 7729638
Tumor necrosis factor receptors in patients with chronic hepatitis B virus infection.
May 1995

17/6/33
08442117 95044704 PMID: 7956620
Serum levels of soluble immune factors and pathogenesis of chronic hepatitis C, and their relation to therapeutic response to interferon-alpha.
Nov 1994

17/6/34
08252867 95012128 PMID: 7927247
Changes in cytokine production during therapy with granulocyte-macrophage colony-stimulating factor in patients with chronic hepatitis B.
Nov 1994

17/6/35
08250328 95008348 PMID: 7923888
Circulating proinflammatory cytokines (IL-1 beta, TNF-alpha, and IL-6) and IL-1 receptor antagonist (IL-1Ra) in fulminant hepatic failure and acute hepatitis.
Oct 1994

17/6/36
08054554 94132539 PMID: 8301059
Pilot study of natural human interleukin-2 in patients with chronic hepatitis B. Immunomodulatory and antiviral effects.
Sep 1993

17/6/37
07806424 92371954 PMID: 1324217
High concentrations of soluble tumor necrosis factor receptors in ascites.
Sep 1992
? t s17/9/12,19,22,24,25,27,31,32,33

17/9/12
DIALOG(R)File 155:MEDLINE(R)

10602254 20208742 PMID: 10746953
Acute hepatotoxicant exposure induces TNFR-mediated hepatic injury and cytokine/apoptotic gene expression.
Horn TL; O'Brien TD; Schook LB; Rutherford MS
Department of Veterinary PathoBiology, University of Minnesota, St. Paul 55108, USA.
Toxicological sciences (UNITED STATES) Mar 2000, 54 (1) p262-73, ISSN 1096-6080 Journal Code: CZ1
Contract/Grant No.: ES04348, ES, NIEHS; ES08395, ES, NIEHS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Subfile: INDEX MEDICUS
Tumor necrosis factor receptor knockout (TNFR KO) mice were used to examine the role of tumor necrosis factor-alpha (TNFalpha) signaling during acute hepatotoxicant exposure. Mice were exposed intraperitoneally (ip) to either vehicle, phosphate-buffered saline (PBS), or dimethylnitrosamine (DMN, 100 mg/kg) for 24 h. Histological evaluation showed that DMN-treated TNFR-2 KO mice had increased liver damage compared to wild type (WT), TNFR-1 KO, or TNFR double KO (DKO) mice. Also, 3 of 8 TNFR-2 KO mice died following DMN treatment, suggesting that hepatic TNFR-2 signaling produces protective responses that counteract TNFR-1-mediated damage. DMN-induced cellular infiltration was absent in TNFR-1-deficient mice, indicating that infiltrating cells do not exacerbate acute hepatotoxic events. In separate experiments, mice were exposed ip to either DMN (5.0 or 100 mg/kg), carbon tetrachloride (CCl4, 0.3 or 1.0 ml/kg), or corresponding PBS/corn oil controls for 6 or 24 h to compare the hepatic mRNA expression of cytokine- and apoptotic-associated genes. Following 24 h of DMN (100 mg/kg) or 6-24 h of CCl4 treatment, hepatic transcripts for TNFalpha, interferon (IFN)-gamma, IL (interleukin)-1RI, and transforming growth factor (TGF)-betaRII were induced. Hepatotoxicant-treated WT and TNFR DKO mice induced liver transcripts for the pro- and anti-apoptotic genes, Bax and Bcl-X(L), respectively, indicating TNF-independent gene activation. The anti-apoptotic gene, Bfl-1, was highly expressed in CCl4-treated, TNFR-positive strains, but minimally expressed in TNFR DKO mice, suggesting that hepatic Bfl-1 is TNF-regulated. Taken together, these data show that acute hepatotoxicant exposure is followed by upregulation of liver cytokine, cytokine receptor, and apoptotic transcripts, and that TNFalpha regulates various aspects of liver inflammation and injury in a TNFR-specific fashion.
Tags: Animal; Female; Male; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Descriptors: *Apoptosis--genetics--GE; *Cytokines--genetics--GE; *Gene Expression--genetics--GE; *Hepatitis, Toxic--genetics--GE; *Receptors, Tumor Necrosis Factor--genetics--GE; Alkylating Agents--toxicity--TO; Carbon Tetrachloride Poisoning--genetics--GE; Carbon Tetrachloride Poisoning--pathology--PA; Dimethylnitrosamine--toxicity--TO; Hepatitis, Toxic--pathology--PA; Liver--pathology--PA; Mice; Mice, Knockout; RNA, Messenger--biosynthesis--BI; Receptors, Cytokine--genetics--GE; Receptors, Cytokine--metabolism--ME
CAS Registry No.: 0 (Alkylating Agents); 0 (Cytokines); 0 (RNA, Messenger); 0 (Receptors, Cytokine); 0 (Receptors, Tumor Necrosis Factor); 62-75-9 (Dimethylnitrosamine)
Record Date Created: 20000602

17/9/19
DIALOG(R)File 155:MEDLINE(R)

09864590 98359682 PMID: 9696493
Pentoxifylline prevents concanavalin A-induced hepatitis by reducing tumor necrosis factor alpha levels and inhibiting adhesion of T lymphocytes to extracellular matrix.
Shirin H; Bruck R; Aeed H; Frenkel D; Kenet G; Zaidel L; Avni Y; Halpern Z; Hershkoviz R
Department of Gastroenterology, The E. Wolfson Medical Center, Holon, Israel.
Journal of hepatology (DENMARK) Jul 1998, 29 (1) p60-7, ISSN 0168-8278 Journal Code: IBS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Subfile: INDEX MEDICUS
BACKGROUND/AIMS: Concanavalin A activates T lymphocytes and causes T cell-mediated hepatic injury in mice. Tumor necrosis factor alpha is a critical mediator in this experimental model. T-cell-mediated liver injury involves the migration of immune cells, notably CD4+ T lymphocytes, into

inflammation in the liver. It is also suggested that both cytokines may be related to the development of HCC.
Tags: Female; Human; Male; Support, Non-U.S. Gov't
Descriptors: *Hepatitis C--immunology--IM; *Interleukin-10--metabolism --ME; *Interleukin-15--metabolism--ME; *Receptors, Tumor Necrosis Factor --metabolism--ME; Adult; Aged; Antiviral Agents--therapeutic use--TU; Carcinoma, Hepatocellular--drug therapy--DT; Carcinoma, Hepatocellular --immunology--IM; Carcinoma, Hepatocellular--virology--VI; Chronic Disease ; Hepatitis C--blood--BL; Hepatitis C--drug therapy--DT; Hepatitis C-Like Viruses--genetics--GE; Interferons--therapeutic use--TU; Interleukin-10 --blood--BL; Interleukin-15--blood--BL; Liver--immunology--IM; Liver Cirrhosis--drug therapy--DT; Liver Cirrhosis--immunology--IM; Liver Cirrhosis--virology--VI; Liver Neoplasms--drug therapy--DT; Liver Neoplasms--immunology--IM; Liver Neoplasms--virology--VI; Middle Age; RNA, Viral--analysis--AN; Receptors, Tumor Necrosis Factor--blood--BL; Receptors, Tumor Necrosis Factor--drug effects--DE; Transaminases --metabolism--ME
CAS Registry No.: 0 (Antiviral Agents); 0 (Interleukin-15); 0 (RNA, Viral); 0 (Receptors, Tumor Necrosis Factor); 130068-27-8 (Interleukin-10); 9008-11-1 (Interferons)
Enzyme No.: EC 2.6.1. (Transaminases)
Record Date Created: 19971023

17/9/24
DIALOG(R)File 155:MEDLINE(R)

09456098 97131716 PMID: 8977217
Involvement of 26-kDa cell-associated TNF-alpha in experimental hepatitis and exacerbation of liver injury with a matrix metalloproteinase inhibitor.
Solorzano CC; Ksontini R; Pruitt JH; Hess PJ; Edwards PD; Kaibara A; Abouhamze A; Auffenberg T; Galardy RE; Vauthey JN; Copeland EM; Edwards CK; Lauwers GY; Clare-Salzler M; MacKay SL; Moldawer LL; Lazarus DD
Department of Surgery, University of Florida College of Medicine, Gainesville 32610, USA.
Journal of immunology (UNITED STATES) Jan 1 1997, 158 (1) p414-9, ISSN 0022-1767 Journal Code: IFB
Contract/Grant No.: GM-40586, GM, NIGMS; GM-52532, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Subfile: AIM; INDEX MEDICUS
TNF-alpha is a pleiotropic cytokine that exists both as a 26-kDa cell-associated and a 17-kDa soluble form. Recently, a class of matrix metalloproteinase inhibitors has been identified that can prevent the processing by TNF convertase of 26-kDa TNF-alpha to its 17-kDa form and can reduce mortality from normally lethal doses of D-galactosamine plus LPS (D-GalN/LPS). Here we report that a matrix metalloproteinase inhibitor, GM-6001, improves survival but does not protect against liver injury from D-GalN/LPS-induced shock in the mouse. In Con A-induced hepatitis, GM-6001 actually exacerbates hepatocellular necrosis and apoptosis despite greater than 90% reduction in plasma TNF-alpha concentrations. Treatment with GM-6001 also has minimal effect on the concentration of membrane-associated TNF-alpha in the livers of animals with Con A induced hepatitis. In contrast, a TNF binding protein (TNF-bp), which neutralizes both membrane-associated and soluble TNF-alpha, prevents D-GalN/LPS- and Con A-induced hepatitis. Our studies suggest that cell-associated TNF-alpha plays a role in the hepatocellular necrosis and apoptosis that accompany D-GalN/LPS- or Con A-induced hepatitis, and that matrix metalloproteinase inhibitors are ineffective in preventing this hepatic injury.
Tags: Animal; Support, U.S. Gov't, P.H.S.
Descriptors: *Dipeptides--toxicity--TO; *Hepatitis, Toxic--pathology--PA; *Metalloendopeptidases--antagonists and inhibitors--AI; *Protease Inhibitors--toxicity--TO; *Tumor Necrosis Factor--chemistry--CH; *Tumor Necrosis Factor--toxicity--TO; Concanavalin A--toxicity--TO; Drug Synergism ; Galactosamine--chemistry--CH; Galactosamine--toxicity--TO; Hepatitis, Toxic--drug therapy--DT; Hepatitis, Toxic--mortality--MO; Lipopolysaccharides--toxicity--TO; Liver--drug effects--DE; Liver--injuries--IN; Mice; Mice, Inbred C57BL; Receptors, Tumor Necrosis Factor--blood--BL; Tumor Necrosis Factor--analysis--AN
CAS Registry No.: 0 (Dipeptides); 0 (GM 6001); 0 (Lipopolysaccharides); 0 (Protease Inhibitors); 0 (Receptors, Tumor Necrosis Factor); 0 (Tumor Necrosis Factor); 11028-71-0 (Concanavalin A) ; 7535-00-4 (Galactosamine)
Enzyme No.: EC 3.4.24 (Metalloendopeptidases)
Record Date Created: 19970130

Subfile: AIM; INDEX MEDICUS

TNF-alpha is a pleiotropic cytokine that exists both as a 26-kDa cell-associated and a 17-kDa soluble form. Recently, a class of matrix metalloproteinase inhibitors has been identified that can prevent the processing by TNF convertase of 26-kDa TNF-alpha to its 17-kDa form and can reduce mortality from normally lethal doses of D-galactosamine plus LPS (D-GalN/LPS). Here we report that a matrix metalloproteinase inhibitor, GM-6001, improves survival but does not protect against liver injury from D-GalN/LPS-induced shock in the mouse. In Con A-induced hepatitis, GM-6001 actually exacerbates hepatocellular necrosis and apoptosis despite greater than 90% reduction in plasma TNF-alpha concentrations. Treatment with GM-6001 also has minimal effect on the concentration of membrane-associated TNF-alpha in the livers of animals with Con A induced hepatitis. In contrast, a TNF binding protein (TNF-bp), which neutralizes both membrane-associated and soluble TNF-alpha, prevents D-GalN/LPS- and Con A-induced hepatitis. Our studies suggest that cell-associated TNF-alpha plays a role in the hepatocellular necrosis and apoptosis that accompany D-GalN/LPS- or Con A-induced hepatitis, and that matrix metalloproteinase inhibitors are ineffective in preventing this hepatic injury.

Tags: Animal; Support, U.S. Gov't, P.H.S.

Descriptors: *Dipeptides--toxicity--TO; *Hepatitis, Toxic--pathology--PA; *Metalloendopeptidases--antagonists and inhibitors--AI; *Protease Inhibitors--toxicity--TO; *Tumor Necrosis Factor--chemistry--CH; *Tumor Necrosis Factor--toxicity--TO; Concanavalin A--toxicity--TO; Drug Synergism ; Galactosamine--chemistry--CH; Galactosamine--toxicity--TO; Hepatitis, Toxic--drug therapy--DT; Hepatitis, Toxic--mortality--MO; Lipopolysacchari des--toxicity--TO; Liver--drug effects--DE; Liver--injuries--IN; Mice; Mice, Inbred C57BL; Receptors, Tumor Necrosis Factor--blood--BL; Tumor Necrosis Factor--analysis--AN

CAS Registry No.: 0 (Dipeptides); 0 (GM 6001); 0 (Lipopolysaccharides); 0 (Protease Inhibitors); 0 (Receptors, Tumor Necrosis Factor); 0 (Tumor Necrosis Factor); 11028-71-0 (Concanavalin A) ; 7535-00-4 (Galactosamine)

Enzyme No.: EC 3.4.24 (Metalloendopeptidases)

Record Date Created: 19970130

14/9/118

DIALOG(R)File 155:MEDLINE(R)

08250328 95008348 PMID: 7923888

Circulating proinflammatory cytokines (IL-1 beta, TNF-alpha, and IL-6) and IL-1 receptor antagonist (IL-1Ra) in fulminant hepatic failure and acute hepatitis.

Sekiyama KD; Yoshiba M; Thomson AW

Pittsburgh Transplantation Institute, PA.

Clinical and experimental immunology (ENGLAND) Oct 1994, 98 (1) p71-7, ISSN 0009-9104 Journal Code: DD7

Contract/Grant No.: DK 29961-09, DK, NIDDK

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Subfile: INDEX MEDICUS

Fulminant hepatic failure (FHF) is characterized by massive necroinflammation of the liver tissue and is associated with high mortality. Serum concentrations of IL-1 beta, tumour necrosis factor-alpha (TNF-alpha), IL-6 and IL-1 receptor antagonist (IL-1Ra) were measured in 30 patients with FHF and in 23 patients with acute hepatitis (AH) before start of treatment and in 23 healthy controls. Levels of all four molecules were increased significantly in FHF compared with AH, in which values were higher than in the healthy controls. High serum levels of IL-1 beta and a significantly reduced ratio of IL-1Ra to IL-1 beta (IL-1Ra/IL-1 beta) were observed in FHF patients who subsequently died compared with subjects who survived. TNF-alpha and IL-6 concentrations were correlated with levels of human hepatocyte growth factor (hHGF), an index of hepatocyte regeneration. Although serum cytokine levels varied considerably between patients within each group studied, it is suggested that the striking elevation in proinflammatory cytokine levels in FHF may reflect both the insufficiency of hepatitis virus elimination and a failure to control a vicious cytokine cascade leading to overwhelming hepatocyte destruction rather than regeneration. The high cytokine levels observed in these patients and the significantly elevated IL-1Ra/IL-1 beta ratio in FHF patients who survived compared with those who did not suggest the possible therapeutic use of cytokine antagonists for the control of this life-threatening disease.

Tags: Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Descriptors: *Cytokines--blood--BL; *Hepatitis, Viral, Human--immunology

liver tissue. Pentoxifylline is a strong suppressor of tumor necrosis factor alpha release and prevents leukocyte adherence to vascular endothelium and down-regulates the expression of intercellular adhesion molecule-1 in monocytes. In this study, we examined the efficacy of pentoxifylline as a potential therapeutic compound for the treatment of concanavalin A hepatitis. METHODS: Balb/c mice were injected with 12 mg/kg concanavalin A with or without a single injection of pentoxifylline (5-300 mg/kg), 2 h prior to concanavalin A administration. Liver damage was evaluated by determining serum levels of liver enzymes and tumor necrosis factor alpha, and hepatic histopathology compared to mice treated with concanavalin A only. We also assessed the effects of pentoxifylline on the adhesive properties of T lymphocytes to fibronectin, as a paradigm for immune cell-extracellular matrix interactions required for migration. Pretreatment with pentoxifylline significantly reduced serum levels of liver enzymes (3800+/-650 vs 150+/-28 IU/l) and tumor necrosis factor alpha (710+/-105 vs 113+/-15 pg/ml) with no evidence of inflammation in histopathologic examination compared to control mice treated with concanavalin A. Pentoxifylline also inhibited the binding of murine T cells to fibronectin. All the effects of pentoxifylline were dose-dependent. CONCLUSIONS: These results indicate that high doses of pentoxifylline can prevent concanavalin A hepatitis by suppression of tumor necrosis factor alpha release and inhibition of T cells adhesion to extracellular matrix.

Tags: Animal; Male

Descriptors: *Hepatitis, Animal--blood--BL; *Hepatitis, Animal --prevention and control--PC; *Pentoxifylline--pharmacology--PD; *T-Lymphocytes--physiology--PH; *Tumor Necrosis Factor --antagonists and inhibitors--AI; *Vasodilator Agents--pharmacology--PD; Cell Adhesion--drug effects--DE; Concanavalin A; Extracellular Matrix; Fibronectins; Hepatitis, Animal--chemically induced--CI; Hepatitis, Animal--pathology--PA; Lactulose--pharmacology--PD; Mice; Mice, Inbred BALB C; Receptors, Tumor Necrosis Factor; Tumor Necrosis Factor--biosynthesis--BI

CAS Registry No.: 0 (Fibronectins); 0 (Receptors, Tumor Necrosis Factor); 0 (Tumor Necrosis Factor); 0 (Vasodilator Agents); 11028-71-0 (Concanavalin A); 4618-18-2 (Lactulose); 6493-05-6 (Pentoxifylline)

Record Date Created: 19980929

17/9/22
DIALOG(R)File 155:MEDLINE(R)

09588981 97466782 PMID: 9328122

Serum levels of IL-10, IL-15 and soluble tumour necrosis factor-alpha (TNF-alpha) receptors in type C chronic liver disease.

Kakumu S; Okumura A; Ishikawa T; Yano M; Enomoto A; Nishimura H; Yoshioka K; Yoshika Y

First Department of Internal Medicine, Aichi Medical University, Japan.

Clinical and experimental immunology (ENGLAND) Sep 1997, 109 (3) p458-63, ISSN 0009-9104 Journal Code: DD7

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Subfile: INDEX MEDICUS

We previously reported that the number of TNF-alpha-producing cells was increased in the liver of patients with type C chronic liver disease. To understand further the pathophysiology of this change, we examined serum levels of two soluble TNF receptors, TNF-alphaRI (p55) and -alphaRII (p75), and IL-10, all of which act as TNF-alpha buffer, and IL-15, a novel cytokine sharing many immunological activities with IL-2, using ELISA methods. We studied control individuals and patients with type C chronic liver disease, including asymptomatic hepatitis C virus (HCV) carriers with persistently normal serum ALT values, and those with chronic hepatitis (CH), liver cirrhosis (LC) and hepatocellular carcinoma (HCC). Both types of sTNF-alphaR closely correlated with disease progression. Patients with LC and HCC had significantly elevated levels for sTNF-alphaRII compared with the other patient groups and controls. Serum IL-10 levels were significantly greater in all chronic liver disease groups than in controls. With respect to IL-15, the values were high in CH, LC and HCC compared with those of controls. Notably, HCC patients showed highest values for both IL-10 and IL-15, with significant differences from the other patient groups. Serial determinations revealed that interferon (IFN) treatment for CH patients resulted in the suppression of circulating IL-10 and IL-15 levels along with decrease in serum aminotransferase values. Both cytokines remained at decreased levels after cessation of therapy in patients who went into clinical and virological remission. On the other hand, treatment did not affect serum levels of sTNF-alphaRs. These findings indicate that serum levels of these molecules correlated with disease progress in chronic HCV infection, and that IL-10 and IL-15 may reflect the degree of

over its use in a proportion of Crohn's patients with concurrent hepatitis C infection, since there are theoretical risks of accelerated hepatic decompensation due to the immunomodulatory impact of infliximab. We report a patient with both Crohn's disease and ongoing active hepatitis C infection who underwent infliximab therapy, with no worsening of his liver function or PCR status.

Tags: Case Report; Human; Male

Descriptors: *Antibodies, Monoclonal--therapeutic use--TU; *Crohn Disease --complications--CO; *Crohn Disease--drug therapy--DT; *Gastrointestinal Agents--therapeutic use--TU; *Hepatitis C, Chronic--complications--CO; Adult

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Gastrointestinal Agents); 0 (monoclonal antibody cA2)

Record Date Created: 20010314

6/9/6

DIALOG(R)File 155:MEDLINE(R)

10964098 20535798 PMID: 11085348

Comparative tolerability of treatments for inflammatory bowel disease.

Stein RB; Hanauer SB

Department of Medicine, University of Pennsylvania School of Medicine, Philadelphia, USA.

Drug safety (NEW ZEALAND) Nov 2000, 23 (5) p429-48, ISSN 0114-5916. Journal Code: AHQ

Languages: ENGLISH

Document type: Journal Article; Review; Review, Tutorial

Record type: Completed

Subfile: INDEX MEDICUS

Despite limited understanding of therapeutic aetiopathogenesis of ulcerative colitis and Crohn's disease, there is a strong evidence base for the efficacy of pharmacological and biological therapies. It is equally important to recognise toxicity of the medical armamentarium for inflammatory bowel disease (IBD). Sulfasalazine consists of sulfapyridine linked to 5-aminosalicylic acid (5-ASA) via an azo bond. Common adverse effects related to sulfapyridine 'intolerance' include headache, nausea, anorexia, and malaise. Other allergic or toxic adverse effects include fever, rash, haemolytic anaemia, hepatitis, pancreatitis, paradoxical worsening of colitis, and reversible sperm abnormalities. The newer 5-ASA agents were developed to deliver the active ingredient of sulfasalazine while minimising adverse effects. Adverse effects are infrequent but may include nausea, dyspepsia and headache. Olsalazine may cause a secretory diarrhoea. Uncommon hypersensitivity reactions, including worsening of colitis, pancreatitis, pericarditis and nephritis, have also been reported. Corticosteroids are commonly prescribed for treatment of moderate to severe IBD. Despite short term efficacy, corticosteroids have numerous adverse effects that preclude their long term use. Adverse effects include acne, fluid retention, fat redistribution, hypertension, hyperglycaemia, psycho-neurological disturbances, cataracts, adrenal suppression, growth failure in children, and osteonecrosis. Newer corticosteroid preparations offer potential for targeted therapy and less corticosteroid-related adverse effects. Azathioprine and mercaptopurine are associated with pancreatitis in 3 to 15% of patients that resolves upon drug cessation. Bone marrow suppression is dose related and may be delayed. The adverse effects of methotrexate include nausea, leucopenia and, rarely, hypersensitivity pneumonia or hepatic fibrosis. Common adverse effects of cyclosporin include nephrotoxicity, hypertension, headache, gingival hyperplasia, hyperkalaemia, paresthesias, and tremors. These adverse effects usually abate with dose reduction or cessation of therapy. Seizures and opportunistic infections have also been reported. Antibacterials are commonly employed as primary therapy for Crohn's disease. Common adverse effects of metronidazole include nausea and a metallic taste. Peripheral neuropathy can occur with prolonged administration. Ciprofloxacin and other antibacterials may be beneficial in those intolerant to metronidazole. Newer immunosuppressive agents previously reserved for transplant recipients are under investigation for IBD. Tacrolimus has an adverse effect profile similar to cyclosporin, and may cause renal insufficiency. Mycophenolate mofetil, a purine synthesis inhibitor, has primarily gastrointestinal adverse effects. Biological agents targeting specific sites in the immunoinflammatory cascade are now available to treat IBD. Infliximab, a chimeric antibody targeting tumour necrosis factor-or has been well tolerated in clinical trials and early postmarketing experience. Additional trials are needed to assess long term adverse effects. (205 Refs.)

Tags: Female; Human; Male; Pregnancy

Descriptors: *Adrenal Cortex Hormones--therapeutic use--TU;

mice. Overt ill-health and viral replication in the spleens of BALB/c mice were increased by in vivo treatment with soluble TNF-alpha receptors to inhibit the activity of this cytokine, whilst antibodies to IL-12 had a similar but more restricted effect C57BL/6 mice were not affected by either treatment, suggesting TNF-alpha and IL-12 are not critical for natural killer cell-mediated restriction of viral replication in the spleen. Soluble TNF-alpha receptors and antibodies to IL-12 also enhanced MCMV titres and numbers of viral antigen-positive cells in the livers of BALB/c mice and TNF-alpha receptors have similar effects in C57BL/6 livers. In contrast, IL-1 receptors improved the health of MCMV-infected BALB/c mice and reduced viral replication and hepatitis at some time-points. Mechanisms which may underlie these changes are discussed.

Tags: Animal; Female; Support, Non-U.S. Gov't

Descriptors: *Cytomegalovirus Infections--immunology--IM; *Interleukin-1 --immunology--IM; *Interleukin-12--immunology--IM; *Muromegalovirus --immunology--IM; *Tumor Necrosis Factor--immunology--IM; Cytomegalovirus --physiology--PH; Cytomegalovirus Infections--pathology--PA; Disease Susceptibility; Liver--pathology--PA; Mice; Mice, Inbred BALB C; Mice, Inbred C57BL; Specific Pathogen-Free Organisms; Virus Replication --immunology--IM

CAS Registry No.: 0 (Interleukin-1); 0 (Interleukin-12); 0 (Tumor Necrosis Factor)

Record Date Created: 19970710

17/9/31

DIALOG(R)File 155:MEDLINE(R)

08763807 95111127 PMID: 7811997

Interferon-alpha induces circulating tumor necrosis factor receptor p55 in humans.

Tilg H; Vogel W; Dinarello CA

Department of Medicine, University Hospital Innsbruck, Austria.

Blood (UNITED STATES) Jan 15 1995, 85 (2) p433-5, ISSN 0006-4971 Journal Code: A8G

Contract/Grant No.: AI-15614, AI, NIAID

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Subfile: AIM; INDEX MEDICUS

In the present studies we investigated the effect of interferon-alpha (IFN alpha) on the release of the soluble (extracellular) form of the tumor necrosis factor p55 receptor (TNFsRp55), because TNFsRp55 is a natural antagonist of tumor necrosis factor (TNF)-induced inflammation and also might be part of the antiinflammatory properties of IFN alpha. Plasma levels of TNFsRp55 were measured by a specific radioimmunoassay in five healthy volunteers and in five patients with chronic hepatitis C treated with IFN alpha. Levels showed a significant increase after a single injection of 5.0 million U IFN alpha in both healthy and hepatitis patient groups. Peak values (3.5 to 4.5 ng/mL) were observed within 12 hours of beginning treatment. Thereafter, levels promptly declined, reaching baseline values within 24 hours. TNF alpha and C-reactive protein (CRP) levels were below the detection limit in the same plasma samples. In addition, IFN alpha suppressed significantly interleukin (IL)-1 alpha-induced TNF alpha protein synthesis by human peripheral blood mononuclear cells. These results suggest that the antiinflammatory properties of IFN alpha may be, in part, also due to the induction and/or release of TNF soluble receptors and the suppression of TNF alpha synthesis.

Tags: Human; Male; Support, U.S. Gov't, P.H.S.

Descriptors: *Hepatitis C--blood--BL; *Hepatitis, Chronic--blood--BL; *Interferon-alpha--pharmacology--PD; *Receptors, Tumor Necrosis Factor --biosynthesis--BI; *Up-Regulation (Physiology)--drug effects--DE; C-Reactive Protein--analysis--AN; Inflammation; Lymphocyte Transformation; Receptors, Tumor Necrosis Factor--genetics--GE; Solubility; Tumor Necrosis Factor--antagonists and inhibitors--AI

CAS Registry No.: 0 (Interferon-alpha); 0 (Receptors, Tumor Necrosis Factor); 0 (Tumor Necrosis Factor); 9007-41-4 (C-Reactive Protein)

Record Date Created: 19950203

17/9/32

DIALOG(R)File 155:MEDLINE(R)

08501372 95246979 PMID: 7729638

Tumor necrosis factor receptors in patients with chronic hepatitis B virus infection.

Marinos G; Naoumov NV; Rossol S; Torre F; Wong PY; Gallati H; Portmann B; Williams R
Institute of Liver Studies, King's College School of Medicine and Dentistry, London, England.
Gastroenterology (UNITED STATES) May 1995, 108 (5) p1453-63, ISSN 0016-5085 Journal Code: FH3
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Subfile: AIM; INDEX MEDICUS

BACKGROUND/AIMS: Patients with chronic hepatitis B infection have elevated plasma tumor necrosis factor (TNF) alpha levels. Two TNF-alpha receptors have been identified, each responsible for distinct TNF-alpha activities. The aim of this study was to evaluate the biological function of the elevated TNF-alpha in chronic hepatitis B virus infection by examining the two TNF signaling pathways in the evolution of hepatitis B-related liver injury. METHODS: The hepatic expression of the two TNF receptors and the corresponding serum levels of the soluble forms of both TNF receptors were determined and correlated with hepatic inflammation and virus replication in 98 chronic hepatitis B surface antigen carriers. Forty hepatitis B e antigen-positive patients were also studied prospectively, while on interferon alfa treatment, to examine the TNF receptor response during viral clearance. RESULTS: In chronic hepatitis B virus infection, the hepatic expression and serum levels of TNF receptors, in particular 75-kilodalton TNF receptor subtype (TNF-R p75), are significantly enhanced in association with hepatic inflammation and hepatocytolysis but not with hepatitis B virus replication. During interferon alfa treatment, a significant increase of soluble TNF-R p75 always precedes the hepatitis B e antigen antibody against hepatitis B e antigen seroconversion in responders to treatment. CONCLUSIONS: In chronic active hepatitis B infection, there is an up-regulation of the TNF receptor system, preferentially the TNF-R p75 signaling pathway, which suggests that the TNF-alpha/TNF receptor system has an important role in the pathogenesis of liver damage and viral clearance.

Tags: Human; Support, Non-U.S. Gov't
Descriptors: *Hepatitis B--metabolism--ME; *Receptors, Tumor Necrosis Factor--metabolism--ME; Chi-Square Distribution; Chronic Disease; Hepatitis B--immunology--IM; Hepatitis B--therapy--TH; Hepatitis B Antibodies --metabolism--ME; Hepatitis B Surface Antigens--metabolism--ME; Hepatitis B Virus--physiology--PH; Hepatitis B e Antigens--metabolism--ME; Immunohistochemistry; Interferon Alfa-2b--therapeutic use--TU; Liver --metabolism--ME; Liver--pathology--PA; Liver--virology--VI; Prospective Studies; Regression Analysis; Signal Transduction; Solubility; Tumor Necrosis Factor--metabolism--ME; Virus Replication
CAS Registry No.: 0 (Hepatitis B Antibodies); 0 (Hepatitis B Surface Antigens); 0 (Hepatitis B e Antigens); 0 (Receptors, Tumor Necrosis Factor); 0 (Tumor Necrosis Factor); 0 (tumor necrosis factor receptor 55); 0 (tumor necrosis factor receptor 75); 99210-65-8 (Interferon Alfa-2b)
Record Date Created: 19950530

17/9/33
DIALOG(R)File 155:MEDLINE(R)

08442117 95044704 PMID: 7956620
Serum levels of soluble immune factors and pathogenesis of chronic hepatitis C, and their relation to therapeutic response to interferon-alpha.
Quiroga JA; Martin J; Pardo M; Carreno V
Hepatology Unit, Fundacion Jimenez Diaz, Madrid, Spain.
Digestive diseases and sciences (UNITED STATES) Nov 1994, 39 (11) p2485-96, ISSN 0163-2116 Journal Code: EAD
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Subfile: AIM; INDEX MEDICUS

To test the role of immune reactivity in the pathogenesis of hepatitis C, serum soluble immune factors were measured in a cohort of 57 patients with chronic hepatitis C, and in 20 healthy subjects. Levels of interleukin-1 beta, granulocyte-macrophage colony-stimulating factor, tumor necrosis factor-alpha, and interleukin-6 were detected in some, but not all, HCV patients and were in general undetectable in healthy subjects. Patients had significantly higher concentrations of neopterin ($P = 0.0026$), beta 2-microglobulin ($P = 0.046$), soluble interleukin-2 receptor ($P = 0.021$), and soluble CD8 ($P < 0.039$), than healthy controls; conversely, interferon-gamma levels were significantly lower ($P = 0.023$). Significant

indicates that the association with TNF*2 is interdependent with HLA DRB1*0301. This is an indication that there is more than one susceptibility allele for type 1 AIH on chromosome 6p21.3.
Tags: Female; Human; Male
Descriptors: *Cytokines--genetics--GE; *Hepatitis, Autoimmune--genetics --GE; *Polymorphism (Genetics)--genetics--GE; Adolescence; Adult; Aged; Alleles; Genetic Predisposition to Disease--genetics--GE; Genotype; HLA-B8 Antigen--genetics--GE; Interleukin-1--genetics--GE; Interleukin-10 --genetics--GE; Linkage (Genetics); Middle Age; Promoter Regions (Genetics) --genetics--GE; Reference Values; Sialoglycoproteins--genetics--GE; Tumor Necrosis Factor--genetics--GE
CAS Registry No.: 0 (Cytokines); 0 (HLA-B8 Antigen); 0 (Interleukin-1); 0 (Sialoglycoproteins); 0 (Tumor Necrosis Factor); 0 (interleukin 1 receptor antagonist protein); 130068-27-8 (Interleukin-10)
Record Date Created: 19991020

5/9/26
DIALOG(R)File 155:MEDLINE(R)

09963260 98394628 PMID: 9727645
Tumor necrosis factor and alcoholic liver disease.
McClain CJ; Barve S; Barve S; Deaciuc I; Hill DB
Division of Digestive Diseases and Nutrition, University of Kentucky Medical Center, Lexington 40536-0084, USA.
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Increased levels of hepatic and serum tumor necrosis factor (TNF) have been documented in animal models of alcoholic liver disease and in human alcoholic liver disease. This dysregulated TNF metabolism has been postulated to play a role in many of the metabolic complications and the liver injury of alcoholic liver disease. One potential therapy for alcoholic liver disease may be agents that downregulate TNF production or block TNF activity. Indeed, agents such as prostaglandins and glucocorticoids (both inhibit TNF production) have been used in both human liver disease and experimental models of liver injury, and anti-TNF antibody has recently been shown to attenuate the hepatotoxicity in an animal model of alcoholic-related liver disease. In this study, we demonstrate that a simple ex vivo system can be used to initially assess potential efficacy of anticytokine agents when administered to humans. Both prednisone and a prostaglandin analog were effective in downregulating TNF and interleukin-8 production. The liver is normally resistant to TNF cytotoxicity. Sensitivity to TNF cytotoxicity is thought to occur when there is inadequate production of hepatic protective factors. In this study, we showed that, when patients with acute alcoholic hepatitis were matched with trauma patients for serum levels of interleukin-6, they had similar depressions in the negative acute phase protein, albumin, but markedly different increases in the major acute phase protein, C reactive protein. Patients with alcoholic hepatitis had a very blunted response. We also showed that inhibiting activation of the redox sensitive transcription factor NFkappaB sensitizes to TNF-induced hepatocyte death in vitro. This transcription factor is important for the production of both cytokines and many acute phase protective factors. Several hepatic protective factors are induced by TNF. One possible mechanism for liver injury in alcoholic hepatitis may be inadequate generation of hepatic protective factors. Our future understanding of mechanisms of alcoholic liver disease will involve understanding the balance between noxious and protective factors in the liver, and this should lead to rational therapy for this disease process.
Tags: Animal; Human; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Descriptors: *Hepatitis, Alcoholic--immunology--IM; *Tumor Necrosis Factor--metabolism--ME; Cytokines--antagonists and inhibitors--AI; Cytokines--blood--BL; Dose-Response Relationship, Drug; Down-Regulation (Physiology)--drug effects--DE; Drug Administration Schedule; Hepatitis, Alcoholic--drug therapy--DT; Immune Tolerance--drug effects--DE; Immune Tolerance--immunology--IM; Lipopolysaccharides--immunology--IM; Liver--drug effects--DE; Liver--immunology--IM; Misoprostol--administration and dosage --AD; NF-kappa B--antagonists and inhibitors--AI; NF-kappa B--blood--BL; Prednisone--administration and dosage--AD; Tumor Necrosis Factor --antagonists and inhibitors--AI
CAS Registry No.: 0 (Cytokines); 0 (Lipopolysaccharides); 0

mesalazine is absorbed. Rapid acetylation in the intestinal wall and liver (t1/2beta 0.5 to 2 hours) and transport probably by P-glycoprotein affect mucosal concentrations of mesalazine, which apparently determine clinical response. Any clinical condition influencing the release and topical availability of mesalazine might modify its therapeutic potential. Metronidazole has high (approximately 90%) oral bioavailability, with hepatic elimination characterised by a t1/2beta of 6 to 10 hours and a total clearance of about 4 L/h/kg. Ciprofloxacin is largely excreted unchanged both renally (about 45% of dose) and extrarenally (25%), with a relatively short t1/2beta (3.5 to 7 hours). Thus, renal function affects the systemic availability of ciprofloxacin. Both mercaptopurine and its prodrug azathioprine are metabolised to active compounds (6-thioguanine nucleotides; 6-TGN) by hypoxanthine-guanine phosphoribosyltransferase and to inactive metabolites by the polymorphically expressed thiopurine S-methyltransferase (TPMT) and xanthine oxidase. Patients with low TPMT activity have a higher risk of developing haemopoietic toxicity. Both mercaptopurine and azathioprine have a short t1/2beta (1 to 2 hours), but the t1/2beta of 6-TGN ranges from 3 to 13 days. Therapeutic response seems to be related to 6-TGN concentration. Almost complete bioavailability has been observed after intramuscular and subcutaneous administration of methotrexate, which is predominantly (85%) excreted as unchanged drug with a t1/2beta of up to 50 hours. Thus, renal function is the major determinant for disposition of methotrexate. Cyclosporin is slowly and incompletely absorbed. It is extensively metabolised by CYP3A4/5 in the liver and intestine (median t1/2beta and clearance 7.9 hours and 0.46 L/h/kg, respectively), and inhibitors and inducers of CYP3A4 can modify response and toxicity. Infliximab is predominantly distributed to the vascular compartment and eliminated with a t1/2beta between 10 and 14 days. No accumulation was observed when it was administered at intervals of 4 or 8 weeks. Methotrexate may reduce the clearance of infliximab from serum.
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11661793 21399188 PMID: 11508453
Hepatitis with interface inflammation and IgG, IgM, and IgA anti-double-stranded DNA antibodies following infliximab therapy: comment on the article by Charles et al.
Saleem G; Li SC; MacPherson BR; Cooper SM
Arthritis and rheumatism (United States) Aug 2001, 44 (8) p1966-8, ISSN 0004-3591 Journal Code: 90M
Languages: ENGLISH
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CAS Registry No.: 0 (Antibodies, Antinuclear); 0 (Antibodies, Monoclonal); 0 (Antirheumatic Agents); 0 (IgA); 0 (IgG); 0 (IgM); 0 (monoclonal antibody cA2); 9007-49-2 (DNA)
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Infliximab therapy for Crohn's disease in the presence of chronic hepatitis C infection.
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Treatment of Crohn's disease with infliximab is an important drug therapy for patients with refractory and fistulating disease. There are concerns